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* * * * * * * * * * Welcome to STN International * * * * * * * * *

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NEWS 12 FEB 02 GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13 FEB 06 Patent sequence location (PSL) data added to USGENE
NEWS 14 FEB 10 COMPENDEX reloaded and enhanced
NEWS 15 FEB 11 WTEXTILES reloaded and enhanced
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NEWS 19 FEB 23 MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 20 FEB 23 TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21 FEB 23 Three million new patent records blast AEROSPACE into STN patent clusters

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AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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NEWS LOGIN Welcome Banner and News Items
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Enter NEWS followed by the item number or name to see news on that

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STRUCTURE FILE UPDATES: 20 FEB 2009 HIGHEST RN 1109311-46-7
DICTIONARY FILE UPDATES: 20 FEB 2009 HIGHEST RN 1109311-46-7

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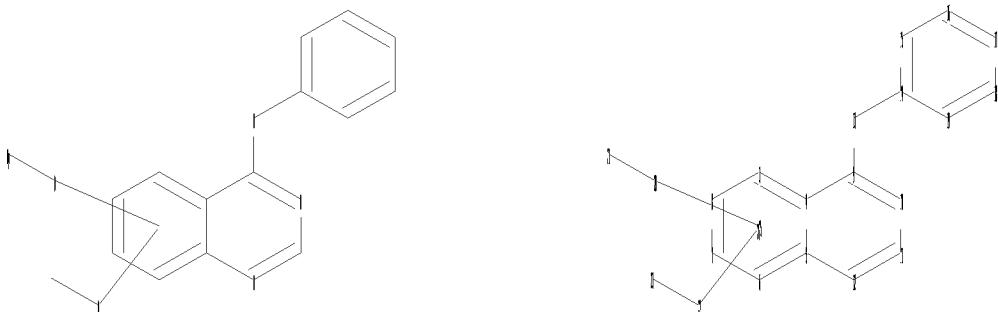
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>
Uploading C:\Program Files\Stnexp\Queries\10573352.str



```
chain nodes :  
13 20 21 22 23  
ring nodes :
```

10/ 573,352

3 4 5 6 7 8 9 10 11 12 14 15 16 17 18 19
chain bonds :
9-13 13-14 20-21 22-23
ring bonds :
3-4 3-8 4-5 4-9 5-6 5-12 6-7 7-8 9-10 10-11 11-12 14-15 14-19 15-16
16-17 17-18 18-19
exact/norm bonds :
9-13 13-14 20-21 22-23
normalized bonds :
3-4 3-8 4-5 4-9 5-6 5-12 6-7 7-8 9-10 10-11 11-12 14-15 14-19 15-16
16-17 17-18 18-19
isolated ring systems :
containing 3 : 14 :

G1:Ak,H

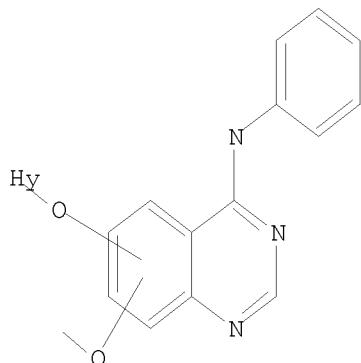
G2:H,CN,X

Hydrogen count :
11:= exact 1
Match level :
3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom
13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:Atom
22:CLASS 23:CLASS 25:Atom 26:Atom
Generic attributes :
21:
Saturation : Saturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 21: Limited
C,C4
N,N1

L1 STRUCTURE UPLOADED

=> d L1
L1 HAS NO ANSWERS
L1 STR



G1 Ak,H

G2 H,CN,X

Structure attributes must be viewed using STN Express query preparation.

=> s 11 full

FULL SEARCH INITIATED 13:26:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 42429 TO ITERATE

100.0% PROCESSED 42429 ITERATIONS
SEARCH TIME: 00.00.01

177 ANSWERS

L2 177 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 185.88 | 186.10 |

FILE 'CAPLUS' ENTERED AT 13:26:49 ON 23 FEB 2009
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FILE COVERS 1907 - 23 Feb 2009 VOL 150 ISS 9
FILE LAST UPDATED: 22 Feb 2009 (20090222/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

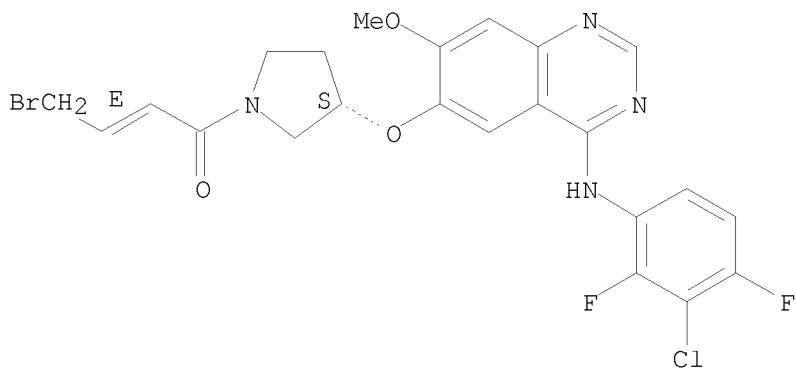
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YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y

L2 ANSWER 1 OF 177 REGISTRY COPYRIGHT 2009 ACS on STN
 RN 1092365-55-3 REGISTRY
 ED Entered STN: 31 Dec 2008
 CN 2-Buten-1-one, 4-bromo-1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-, (2E)- (CA INDEX NAME)
 FS STEREOSEARCH
 MF C23 H20 Br Cl F2 N4 O3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 13:25:53 ON 23 FEB 2009)

FILE 'REGISTRY' ENTERED AT 13:26:03 ON 23 FEB 2009
 L1 STRUCTURE uploaded
 L2 177 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:26:49 ON 23 FEB 2009

FILE 'REGISTRY' ENTERED AT 13:26:55 ON 23 FEB 2009

FILE 'CAPLUS' ENTERED AT 13:26:56 ON 23 FEB 2009

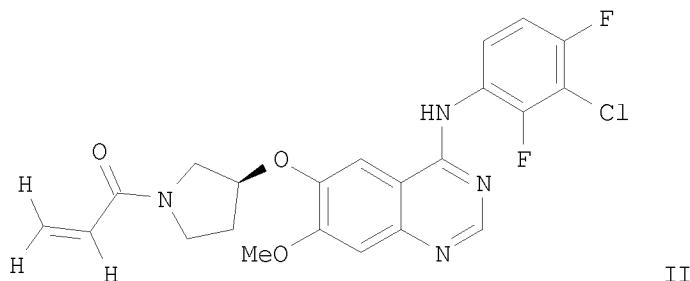
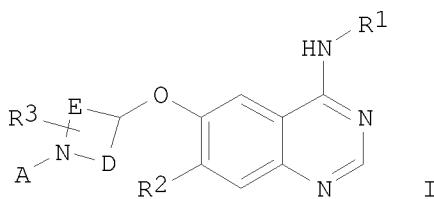
=> s 12

L3 8 L2

=> d L3 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1483773 CAPLUS
DOCUMENT NUMBER: 150:35390
TITLE: Quinazoline-amide derivatives as cancer cell growth inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer
INVENTOR(S): Lee, Kwang-Ok; Cha, Mi Young; Kim, Mi Ra; Jung, Young Hee; Lee, Chang Gon; Kim, Se Young; Bang, Keukchan; Park, Bum Woo; Choi, Bo Im; Chae, Yun Jung; Ko, Mi Young; Kim, Han Kyong; Ahn, Young-Gil; Kim, Maeng Sup; Lee, Gwan Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 128pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|-----------|-----------------|------------|
| WO 2008150118 | A2 | 20081211 | WO 2008-KR3162 | 20080605 |
| WO 2008150118 | A3 | 20090129 | | |
| W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | | |
| KR 2008107294 | A | 20081210 | KR 2008-52867 | 20080605 |
| PRIORITY APPLN. INFO.: | | | KR 2007-54997 | A 20070605 |
| OTHER SOURCE(S): | MARPAT | 150:35390 | | |
| GI | | | | |



AB The invention provides quinazoline-amide derivs. of formula I and their pharmaceutically acceptable salts, (and a pharmaceutical composition comprising same as an active ingredient) which selectively and effectively inhibit the growth of cancer cells induced by the overexpression of an epidermal growth factor receptor and also prevent the development of drug resistance caused by the mutation of EGFR tyrosine kinase. Compds. of formula I wherein A is (un)substituted propynoyl and (un)substituted acryloyl; R1 is (un)substituted (hetero)aryl; R2 is H, OH and (un)substituted C1-6 alkoxy; R2 is H, COOH, C1-6 alkoxycarbonyl and (un)substituted amido; D and E are independently (CH₂)₀₋₆; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by a multi-step procedure (procedure given). All the invention compds. were evaluated for their cancer cell growth inhibitory activity. From the assay, it was determined that II exhibited an IC₅₀ value of 4 nM against A431.

IT
 1092364-02-7P 1092364-03-8P 1092364-04-9P
 1092364-05-0P 1092364-06-1P 1092364-07-2P
 1092364-08-3P 1092364-09-4P 1092364-10-7P
 1092364-11-8P 1092364-14-1P 1092364-15-2P
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 1092364-96-9P 1092364-97-0P 1092364-98-1P

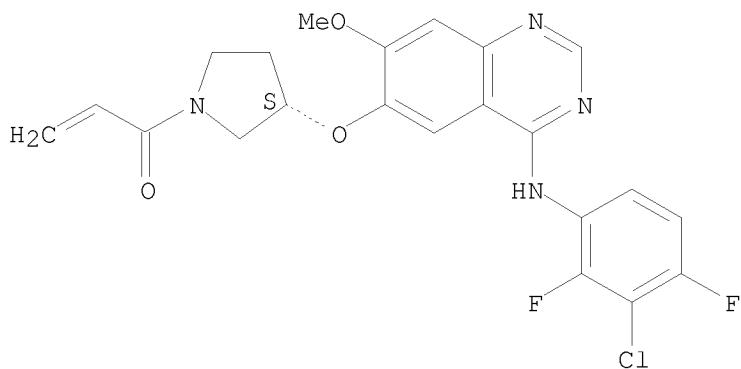
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of quinazoline-amide derivs. as cancer cell growth inhibitors useful in the treatment of cancer)

RN 1092364-02-7 CAPLUS

CN 2-Propen-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

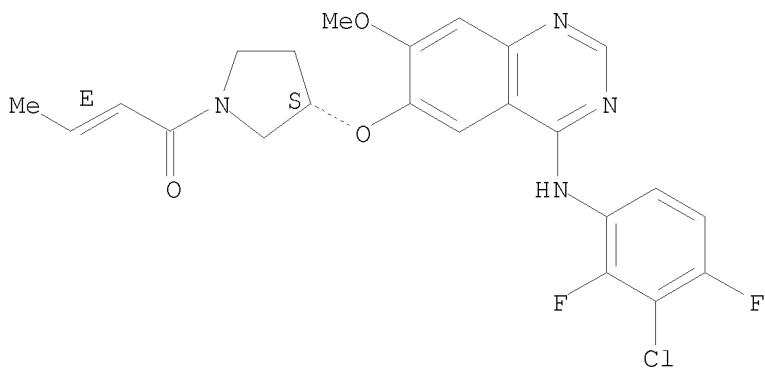


RN 1092364-03-8 CAPLUS

CN 2-Buten-1-one, 1-[(3S)-3-[(4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-, (2E)- (CA INDEX NAME)

Absolute stereochemistry.

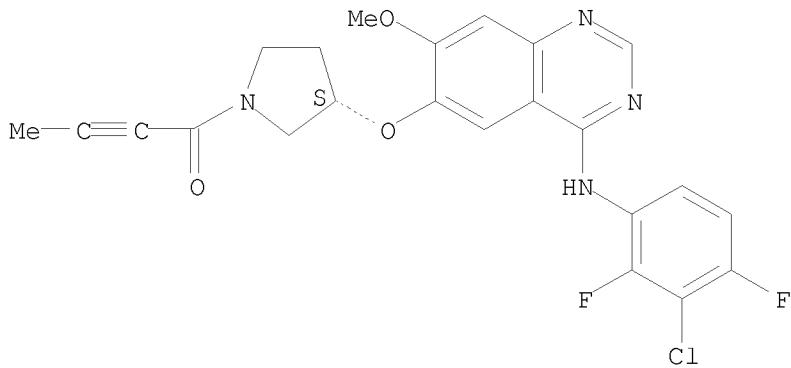
Double bond geometry as shown.



RN 1092364-04-9 CAPLUS

CN 2-Butyn-1-one, 1-[(3S)-3-[(4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

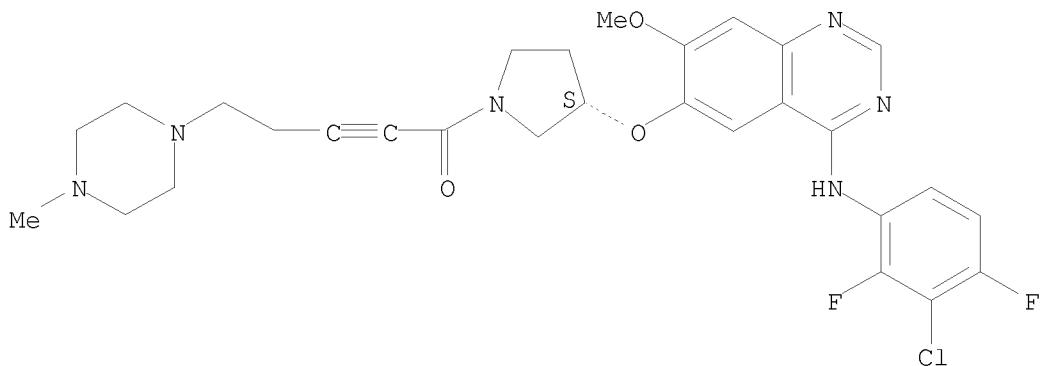
Absolute stereochemistry.



RN 1092364-05-0 CAPLUS

CN 2-Pentyn-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-5-(4-methyl-1-piperazinyl)-(CA INDEX NAME)

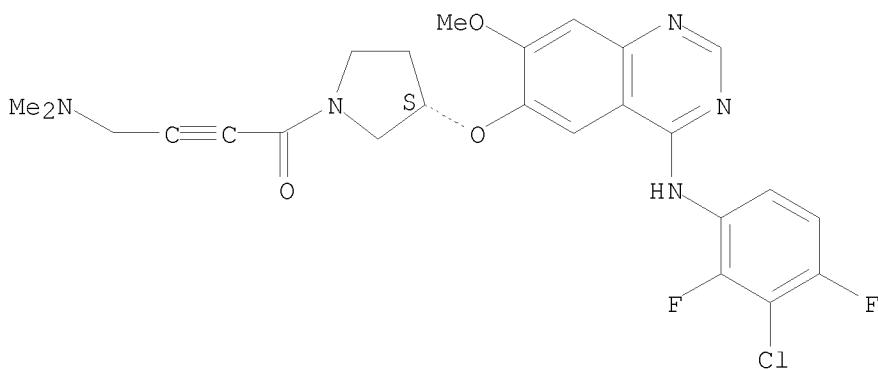
Absolute stereochemistry.



RN 1092364-06-1 CAPLUS

CN 2-Butyn-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-(dimethylamino)-(CA INDEX NAME)

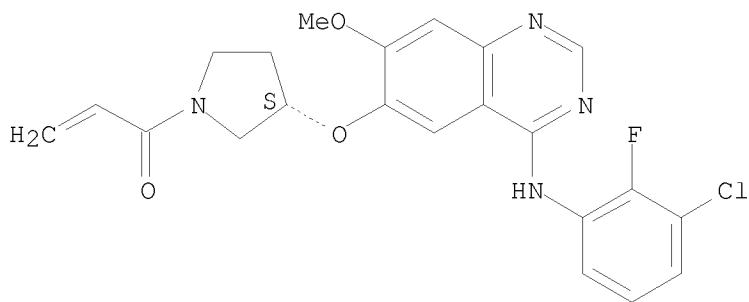
Absolute stereochemistry.



RN 1092364-07-2 CAPLUS

CN 2-Propen-1-one, 1-[(3S)-3-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl)-(CA INDEX NAME)

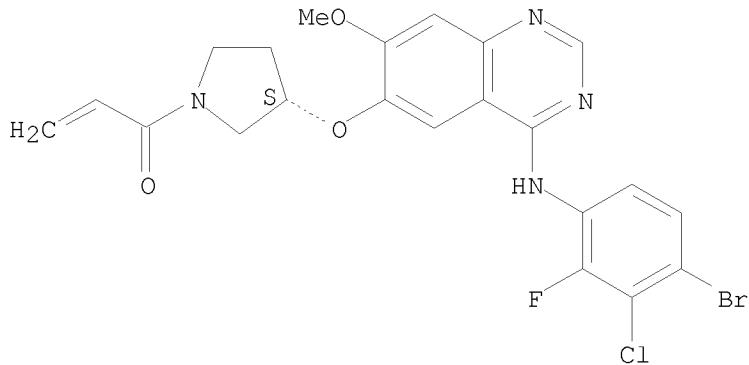
Absolute stereochemistry.



RN 1092364-08-3 CAPLUS

CN 2-Propen-1-one, 1-[(3S)-3-[[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

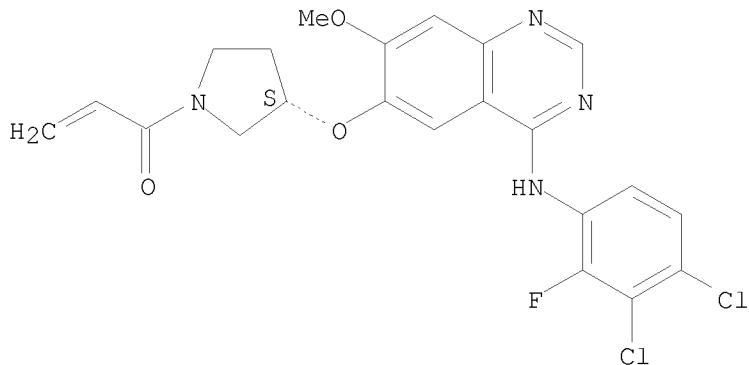
Absolute stereochemistry.



RN 1092364-09-4 CAPLUS

CN 2-Propen-1-one, 1-[(3S)-3-[[4-[(3,4-dichloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

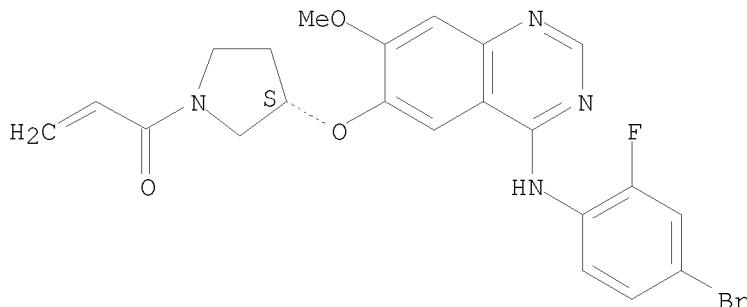
Absolute stereochemistry.



RN 1092364-10-7 CAPLUS

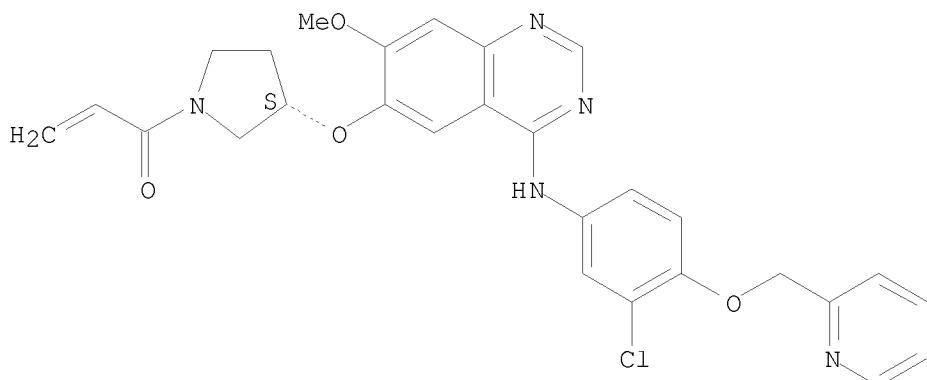
CN 2-Propen-1-one, 1-[(3S)-3-[[4-[(4-bromo-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



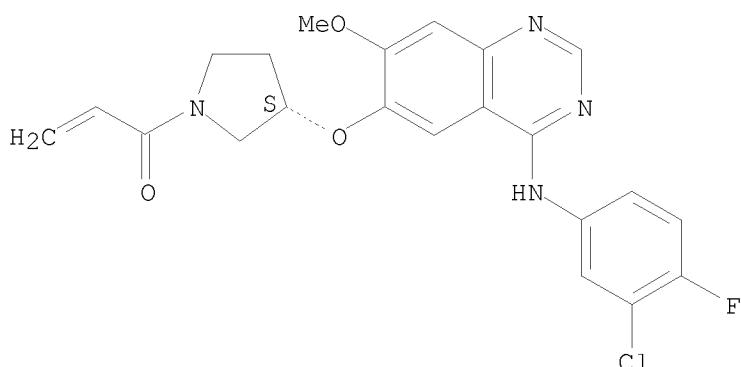
RN 1092364-11-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



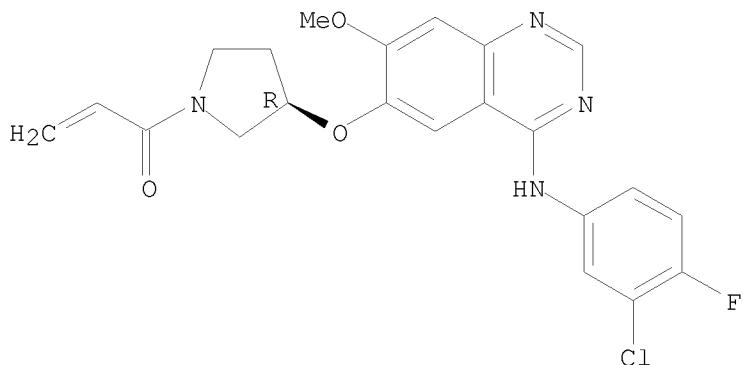
RN 1092364-14-1 CAPLUS
CN 2-Propen-1-one, 1-[(3S)-3-[(4-[3-chloro-4-fluorophenyl]amino)-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 1092364-15-2 CAPLUS
CN 2-Propen-1-one, 1-[(3R)-3-[(4-[3-chloro-4-fluorophenyl]amino)-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl- (CA INDEX NAME)

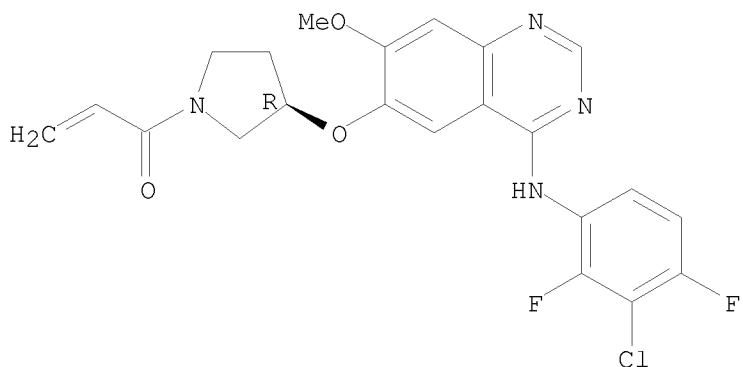
Absolute stereochemistry.



RN 1092364-22-1 CAPLUS

CN 2-Propen-1-one, 1-[(3R)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

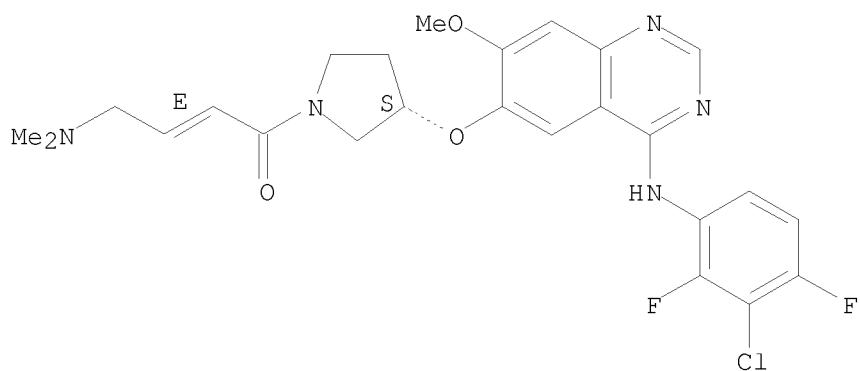


RN 1092364-94-7 CAPLUS

CN 2-Buten-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-(dimethylamino)-, (2E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

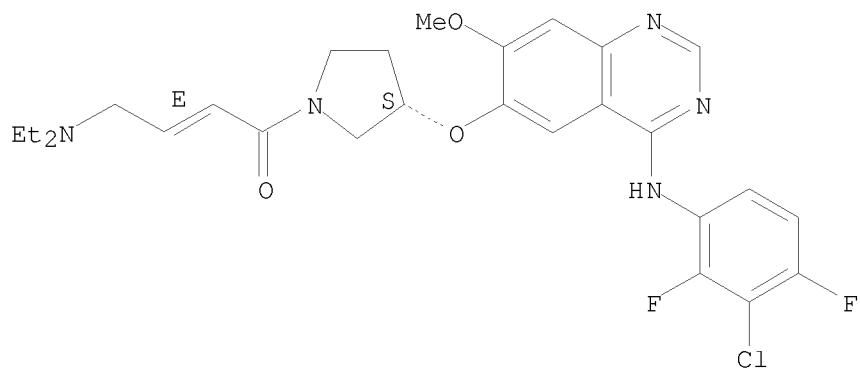


RN 1092364-95-8 CAPLUS

CN 2-Buten-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-(diethylamino)-, (2E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

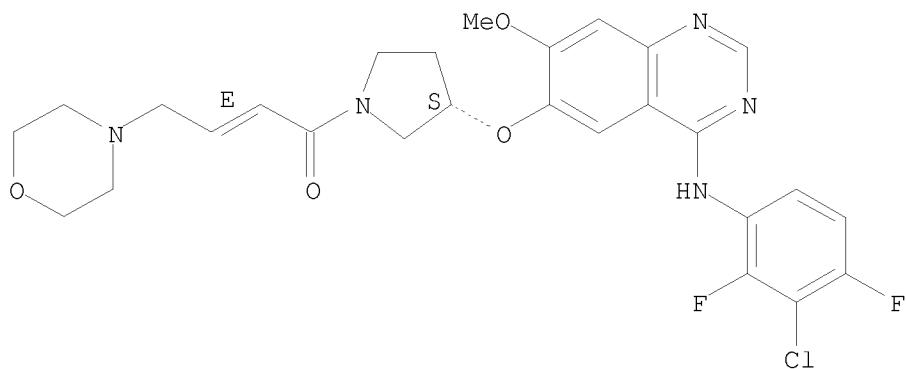


RN 1092364-96-9 CAPLUS

CN 2-Buten-1-one, 1-[(3S)-3-[[4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-(4-morpholinyl)-, (2E)- (CA INDEX NAME)

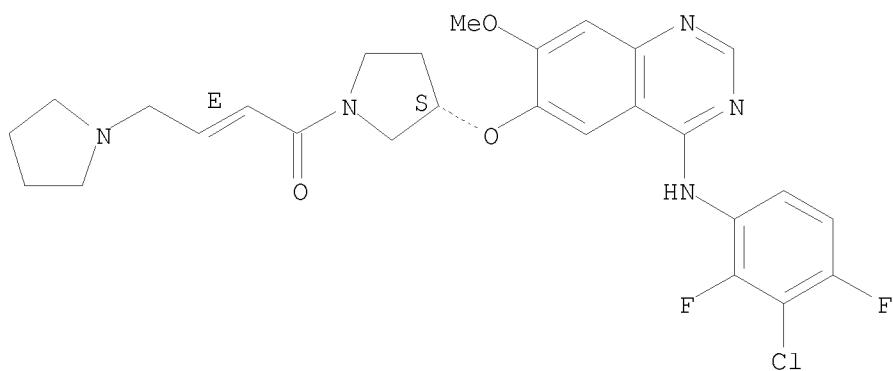
Absolute stereochemistry.

Double bond geometry as shown.



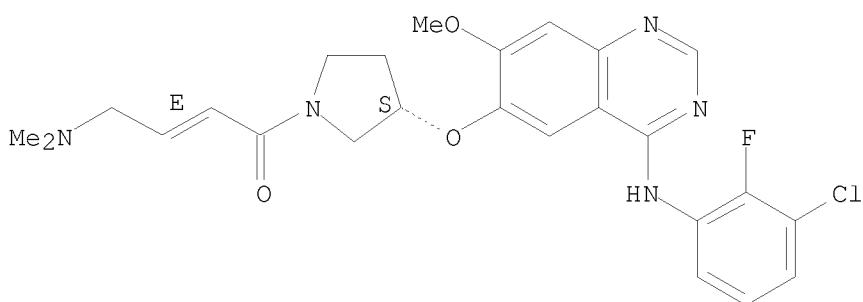
RN 1092364-97-0 CAPLUS
 CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.
 Double bond geometry as shown.



RN 1092364-98-1 CAPLUS
 CN 2-Buten-1-one, 1-[(3S)-3-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-(dimethylamino)-, (2E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



IT 1092365-53-1P 1092365-55-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

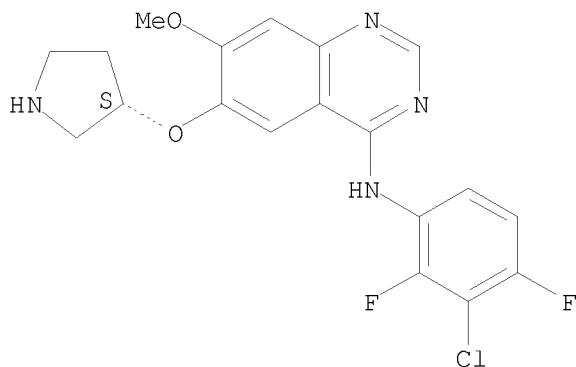
(Reactant or reagent)

(intermediate; preparation of quinazoline-amide derivs. as cancer cell growth inhibitors useful in the treatment of cancer)

RN 1092365-53-1 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2,4-difluorophenyl)-7-methoxy-6-[(3S)-3-pyrrolidinyloxy]- (CA INDEX NAME)

Absolute stereochemistry.

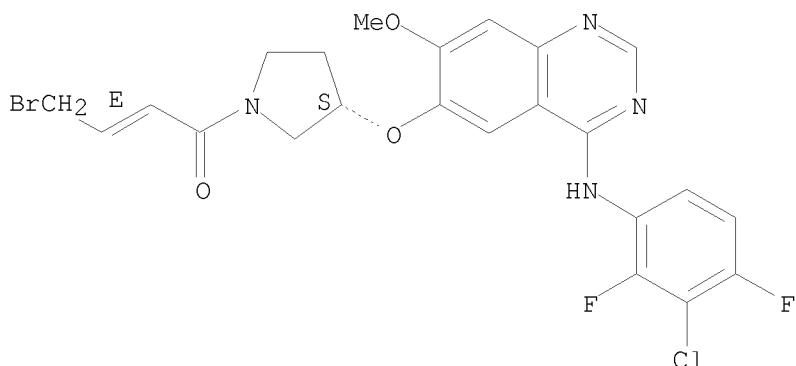


RN 1092365-55-3 CAPLUS

CN 2-Buten-1-one, 4-bromo-1-[(3S)-3-[(4-[(3-chloro-2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-pyrrolidinyl]-, (2E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:227766 CAPLUS

DOCUMENT NUMBER: 146:295946

TITLE: Preparation of quinazolines as EGFR tyrosine kinase inhibitors

INVENTOR(S): Himmelsbach, Frank; Jung, Birgit

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 48pp.

CODEN: PIXXD2

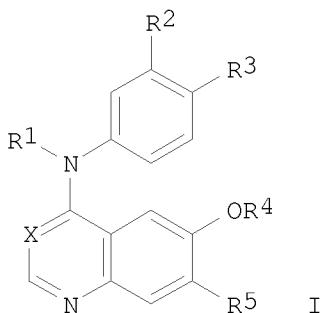
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| ----- | ----- | ----- | ----- | ----- |
| WO 2007023073 | A2 | 20070301 | WO 2006-EP65000 | 20060803 |
| WO 2007023073 | A3 | 20070518 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | | |
| CA 2619037 | A1 | 20070301 | CA 2006-2619037 | 20060803 |
| EP 1919900 | A2 | 20080514 | EP 2006-778135 | 20060803 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| JP 2009506990 | T | 20090219 | JP 2008-527427 | 20060803 |
| PRIORITY APPLN. INFO.: | | | EP 2005-107679 | A 20050822 |
| | | | WO 2006-EP65000 | W 20060803 |
| OTHER SOURCE(S): GI | CASREACT 146:295946; MARPAT 146:295946 | | | |



AB Title compds. [I; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, OH, alkoxy, alkenyl, alkynyl, cyano, NO₂, NH₂, fluorinated Me, MeO; R3 = H, F, Cl, Br, Me, CF₃; R4 = (substituted) cyclobutyl, cyclopentyl, cyclohexyl; R5 = H, F, Cl, Br, OH, alkoxy, fluorinated MeO, EtO, etc.; X = cyano-substituted methine, N], were prepared. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[1-(hydroxymethylcarbonyl)piperidin-4-yloxy]-7-methoxyquinazoline was prepared by reaction of 4-[(3-chloro-4-fluorophenyl)amino]-6-(piperidin-4-yloxy)-7-methoxyquinazoline dihydrochloride with glycolic acid in the presence of N-ethylisopropylamine and TBTU in CH₂Cl₂ at room temperature. Tested I inhibited

EGF receptor kinase with IC₅₀ <1000 nM preferably <100 nM.

IT 1070244-96-0 1070245-14-5

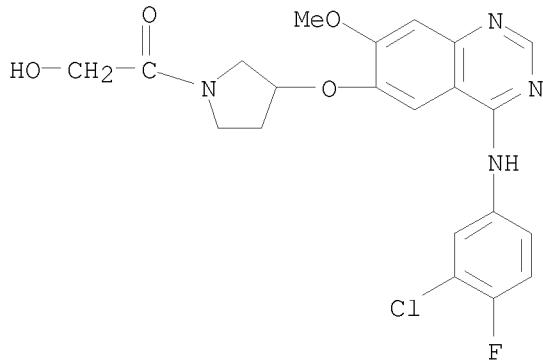
RL: PRPH (Prophetic)

(Preparation of quinazolines as EGFR tyrosine kinase inhibitors)

RN 1070244-96-0 CAPLUS

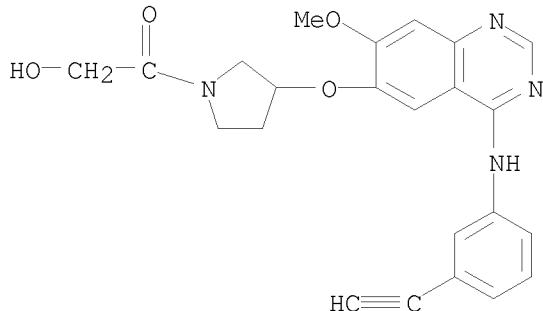
CN Ethanone, 1-[3-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-

quinazolinyl]oxy]-1-pyrrolidinyl]-2-hydroxy- (CA INDEX NAME)



RN 1070245-14-5 CAPLUS

CN Ethanone, 1-[3-[(4-[(3-ethynylphenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-2-hydroxy- (CA INDEX NAME)



L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:300434 CAPLUS

DOCUMENT NUMBER: 142:374111

TITLE: Preparation of proline quinazoline derivatives as antiproliferative agents

INVENTOR(S): Bradbury, Robert Hugh; Halsall, Christopher Thomas; Hennequin, Laurent Francois Andre; Kettle, Jason Grant; Plowright, Alleyn

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Ltd.

SOURCE: PCT Int. Appl., 198 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

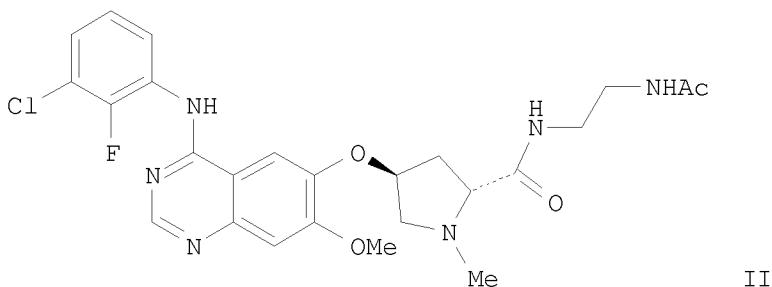
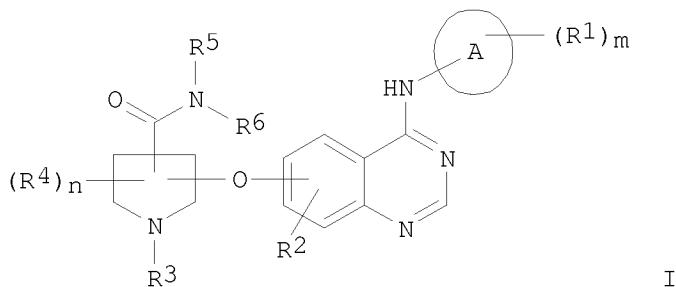
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005030757 | A1 | 20050407 | WO 2004-GB4085 | 20040922 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, | | | | |

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
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 SN, TD, TG

| | | | | |
|--|----|----------|------------------|------------|
| AU 2004276055 | A1 | 20050407 | AU 2004-276055 | 20040922 |
| CA 2540008 | A1 | 20050407 | CA 2004-2540008 | 20040922 |
| EP 1670786 | A1 | 20060621 | EP 2004-768629 | 20040922 |
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| BR 2004014735 | A | 20061121 | BR 2004-14735 | 20040922 |
| CN 1886399 | A | 20061227 | CN 2004-80034739 | 20040922 |
| JP 2007506716 | T | 20070322 | JP 2006-527478 | 20040922 |
| MX 2006003341 | A | 20060608 | MX 2006-3341 | 20060324 |
| US 20070043010 | A1 | 20070222 | US 2006-573352 | 20060324 |
| NO 2006001743 | A | 20060621 | NO 2006-1743 | 20060420 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | GB 2003-22409 | A 20030925 |
| | | | GB 2003-22534 | A 20030926 |
| | | | WO 2004-GB4085 | W 20040922 |

OTHER SOURCE(S): CASREACT 142:374111; MARPAT 142:374111
 GI



AB The invention relates to quinazoline derivs. I [R2 or the substituted pyrrolidinyloxy group is in the 6 or 7 position of the quinazoline ring; A is Ph or pyridyl; m is 0-3; n is 0-2; R1 is halo, cyano, nitro, hydroxy, carboxy, trifluoromethyl, alkyl, alkoxy, alkylsulfonyl, alkylureido, etc.; R2 is H, alkyl, cycloalkyl, cycloalkylalkyl or (un)substituted alkoxy; R3 is H, alkyl, cycloalkyl, alkylthio, alkylsulfinyl, carbamoylalkyl, etc.; R4 is alkyl, alkoxy, cyano, halo, hydroxy or oxo; R5 is H or alkyl; R6 is H, alkyl, alkoxy, heterocyclyl, heteroaryl, etc.; or R5R6N is a ring], including processes for their preparation, pharmaceutical compns. containing them,

and their use as antiproliferative agents in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases. Thus, compound II was prepared by etherification of Boc-protected cis-4-hydroxy-D-proline Me ester with 4-chloro-7-methoxyquinazolin-6-ol and reaction of the product with 3-chloro-2-fluoroaniline in 4.0 M HCl/dioxane and acetonitrile, followed by reductive N-methylation, saponification, and amidation. Compound II showed IC₅₀ = 0.008 nM for inhibition of EGFR tyrosine kinase protein phosphorylation and IC₅₀ = 0.144 nM in the EGFR driven KB cell proliferation assay.

IT 849345-01-3P 849345-02-4P 849345-03-5P
 849345-04-6P 849345-05-7P 849345-06-8P
 849345-07-9P 849345-08-0P 849345-20-6P
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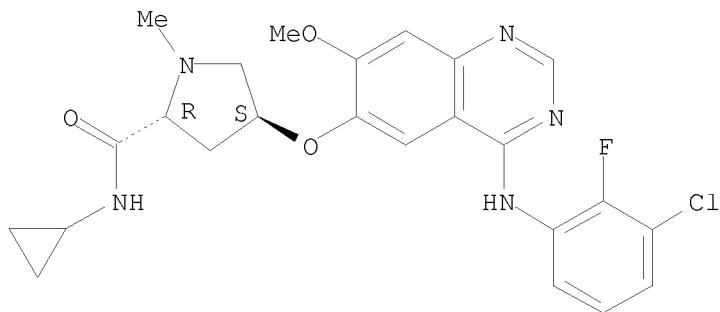
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of proline quinazoline derivs. as antiproliferative agents)

RN 849345-01-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-cyclopropyl-1-methyl-, (2R,4S)- (CA INDEX NAME)

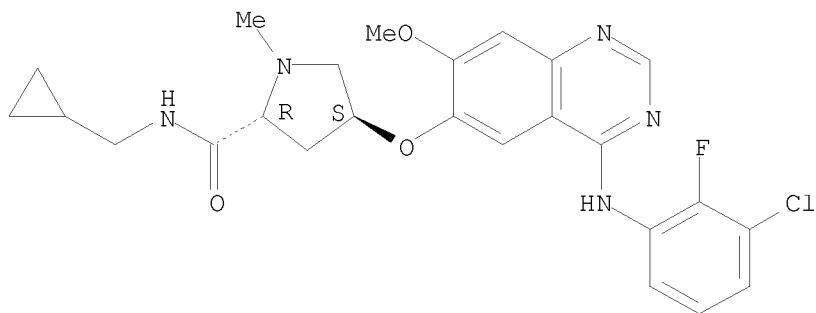
Absolute stereochemistry.



RN 849345-02-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[3-chloro-2-fluorophenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N-(cyclopropylmethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

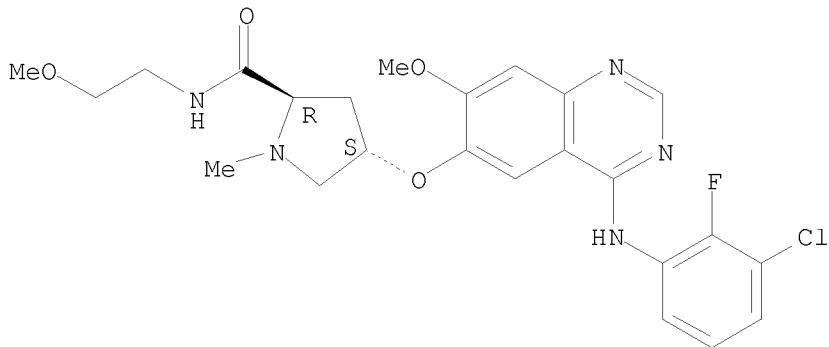
Absolute stereochemistry.



RN 849345-03-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[3-chloro-2-fluorophenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N-(2-methoxyethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

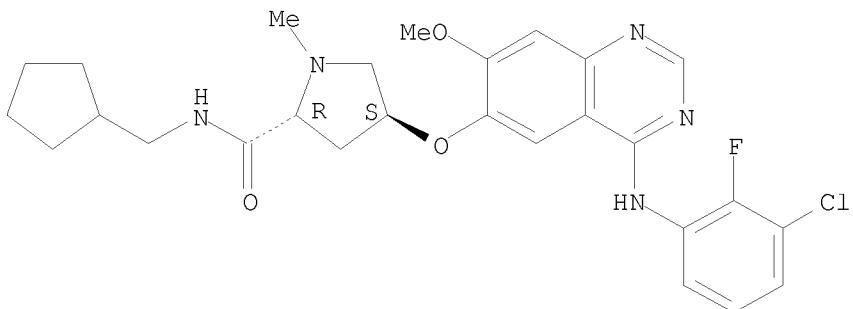
Absolute stereochemistry.



RN 849345-04-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[3-chloro-2-fluorophenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N-(cyclopentylmethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

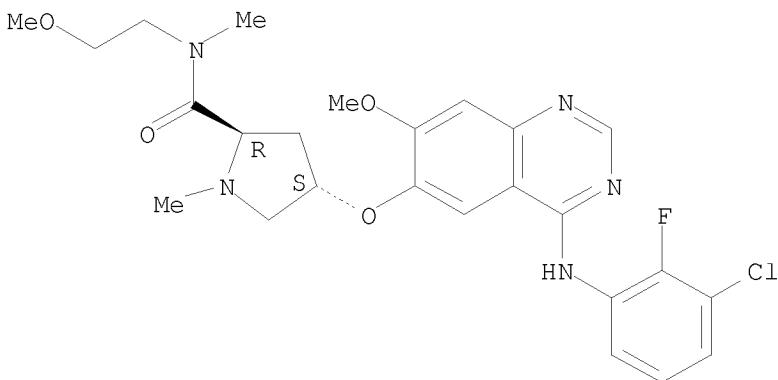
Absolute stereochemistry.



RN 849345-05-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(2-methoxyethyl)-, N,1-dimethyl-, (2R,4S)- (CA INDEX NAME)

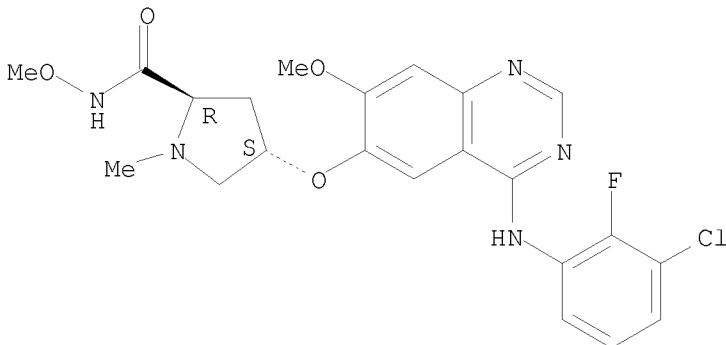
Absolute stereochemistry.



RN 849345-06-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-methoxy-1-methyl-, (2R,4S)- (CA INDEX NAME)

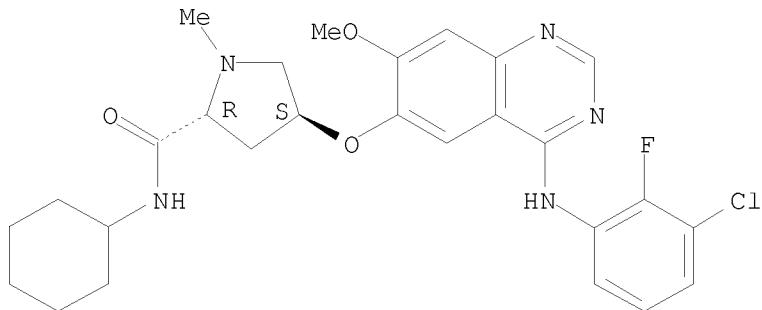
Absolute stereochemistry.



RN 849345-07-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-cyclohexyl-1-methyl-, (2R,4S)- (CA INDEX NAME)

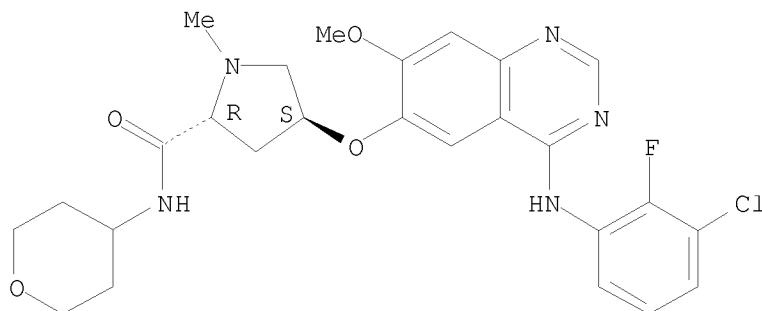
Absolute stereochemistry.



RN 849345-08-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, (2R,4S)- (CA INDEX NAME)

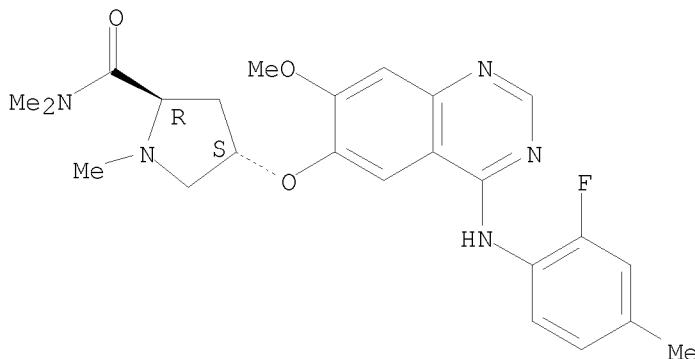
Absolute stereochemistry.



RN 849345-20-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(2-fluoro-4-methylphenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

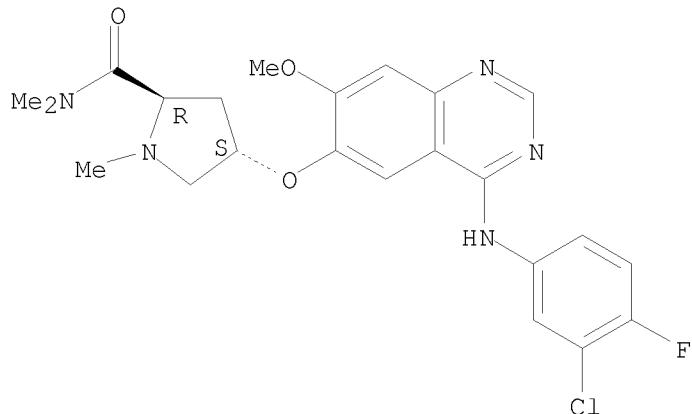
Absolute stereochemistry.



RN 849345-21-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

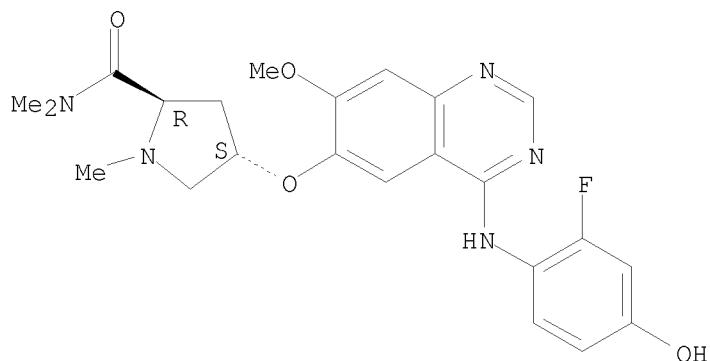
Absolute stereochemistry.



RN 849345-22-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(2-fluoro-4-hydroxyphenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

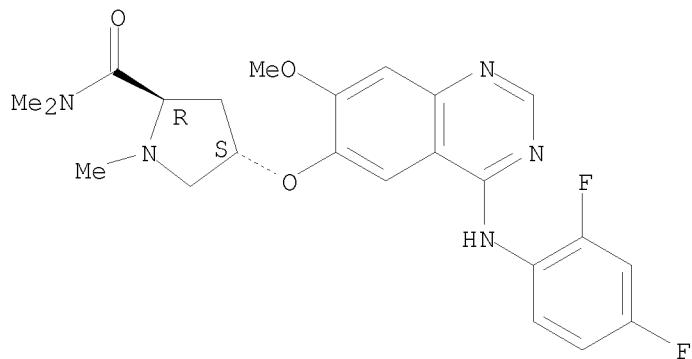
Absolute stereochemistry.



RN 849345-23-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(2,4-difluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

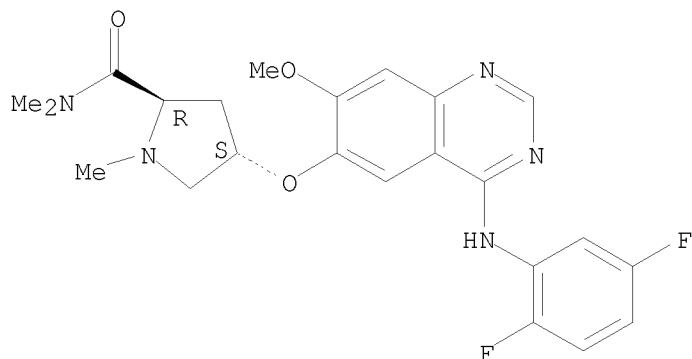
Absolute stereochemistry.



RN 849345-24-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(2,5-difluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

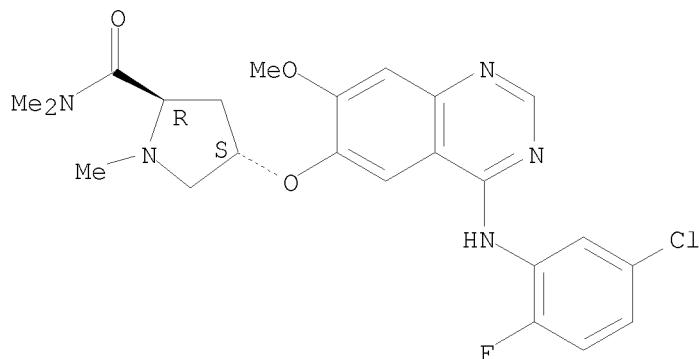
Absolute stereochemistry.



RN 849345-25-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(5-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.

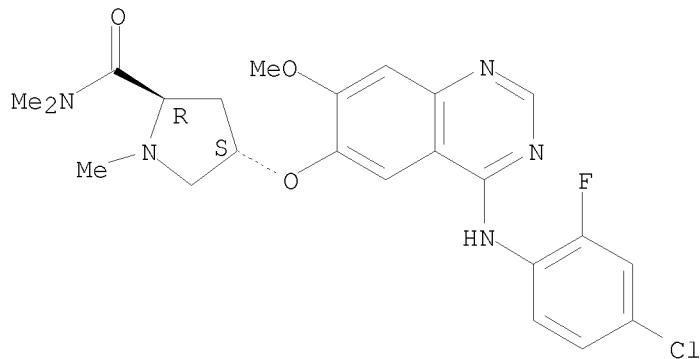


RN 849345-26-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(4-chloro-2-fluorophenyl)amino]-7-methoxy-

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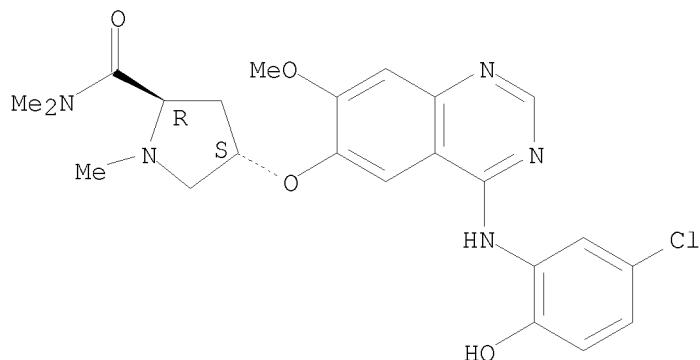
Absolute stereochemistry.



RN 849345-27-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(5-chloro-2-hydroxyphenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

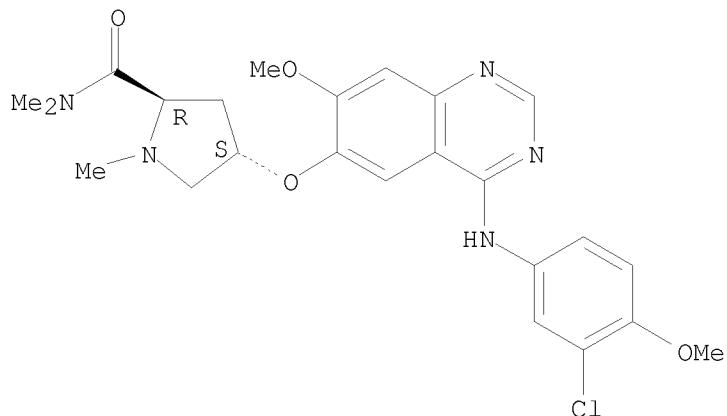
Absolute stereochemistry.



RN 849345-28-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(3-chloro-4-methoxyphenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

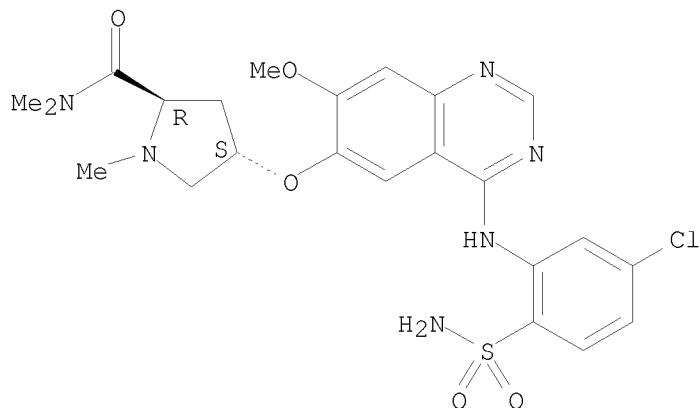
Absolute stereochemistry.



RN 849345-29-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(2-(aminosulfonyl)-5-chlorophenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

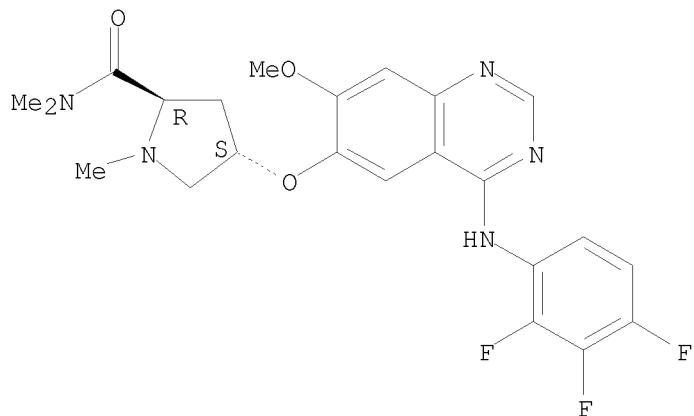
Absolute stereochemistry.



RN 849345-30-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[7-methoxy-4-[(2,3,4-trifluorophenyl)amino]-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

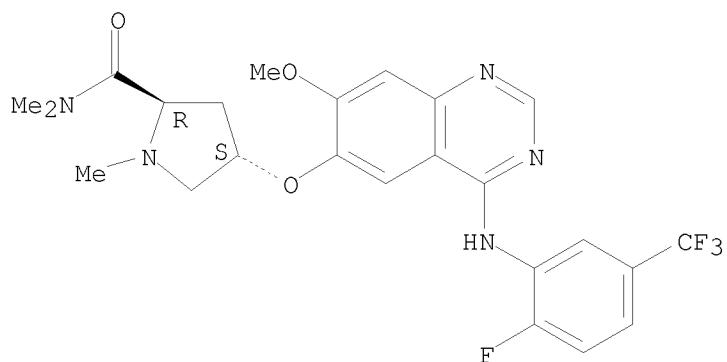
Absolute stereochemistry.



RN 849345-31-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[[2-fluoro-5-(trifluoromethyl)phenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

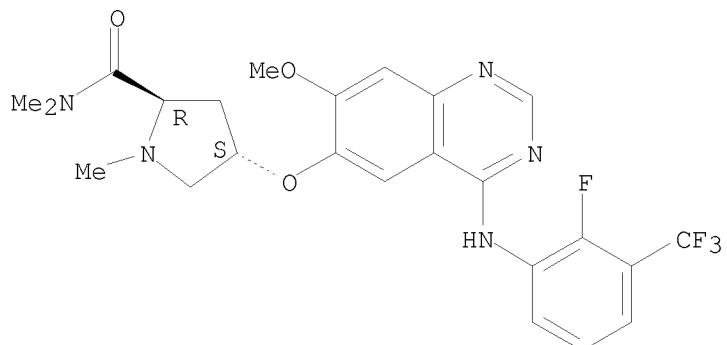
Absolute stereochemistry.



RN 849345-32-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[[2-fluoro-3-(trifluoromethyl)phenyl]amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

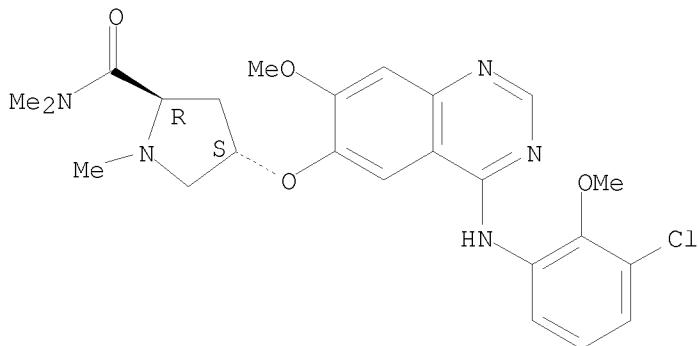
Absolute stereochemistry.



RN 849345-33-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-methoxyphenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

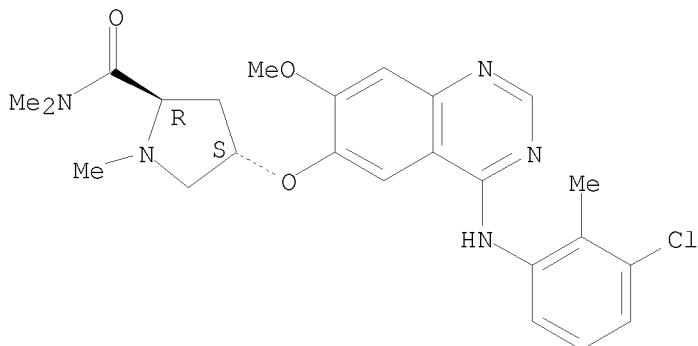
Absolute stereochemistry.



RN 849345-34-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-methylphenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

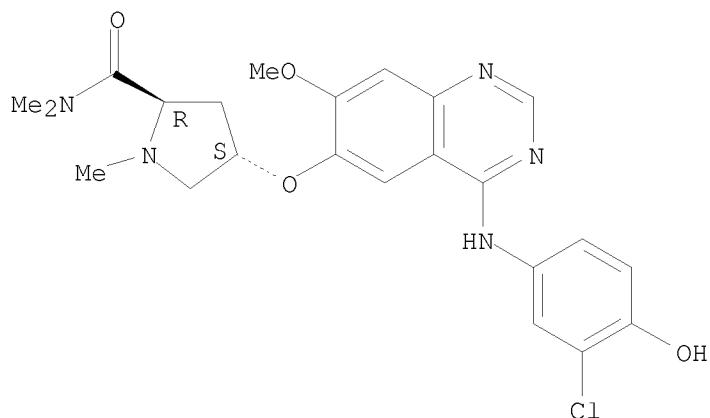
Absolute stereochemistry.



RN 849345-35-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-4-hydroxyphenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

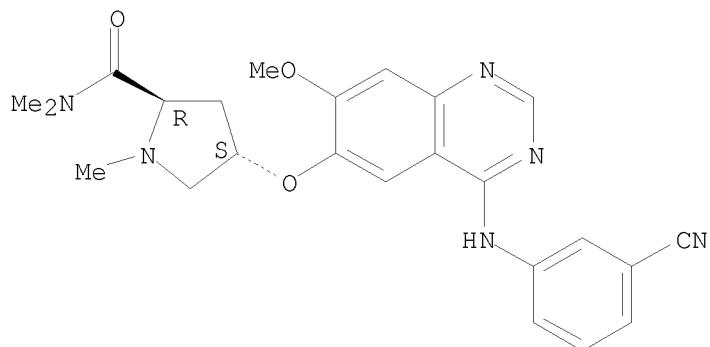
Absolute stereochemistry.



RN 849345-36-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-cyanophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

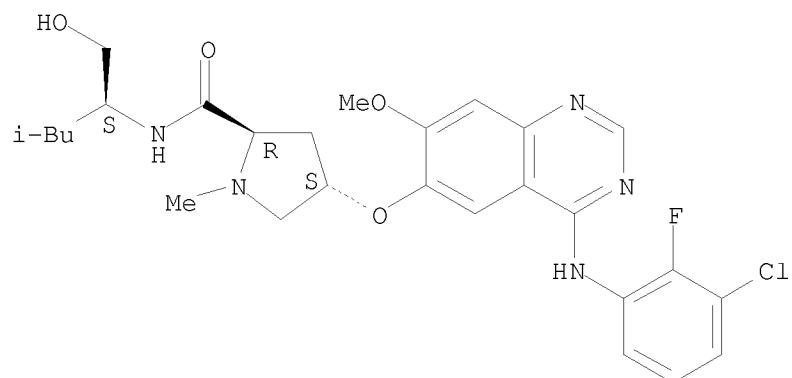
Absolute stereochemistry.



RN 849345-46-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[(1S)-1-(hydroxymethyl)-3-methylbutyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

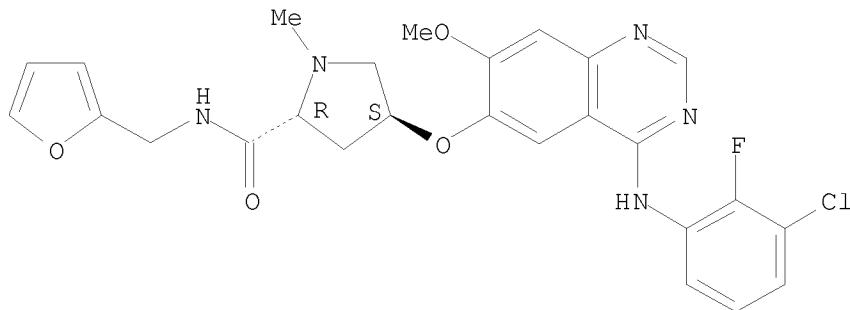
Absolute stereochemistry.



RN 849345-47-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-(2-furanyl methyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

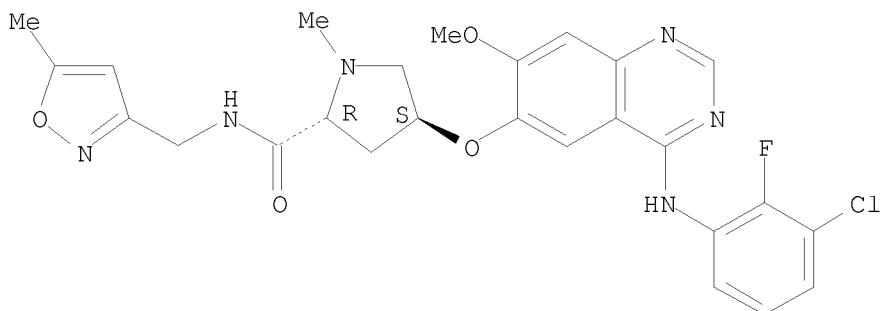
Absolute stereochemistry.



RN 849345-48-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-N-[(5-methyl-3-isoxazolyl)methyl]-, (2R,4S)- (CA INDEX NAME)

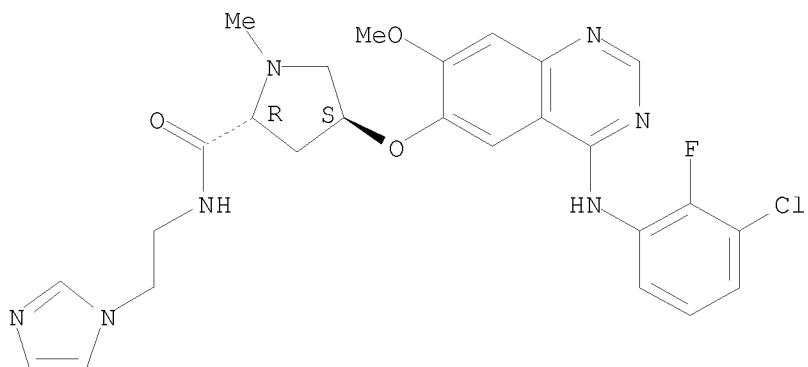
Absolute stereochemistry.



RN 849345-49-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[2-(1H-imidazol-1-yl)ethyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

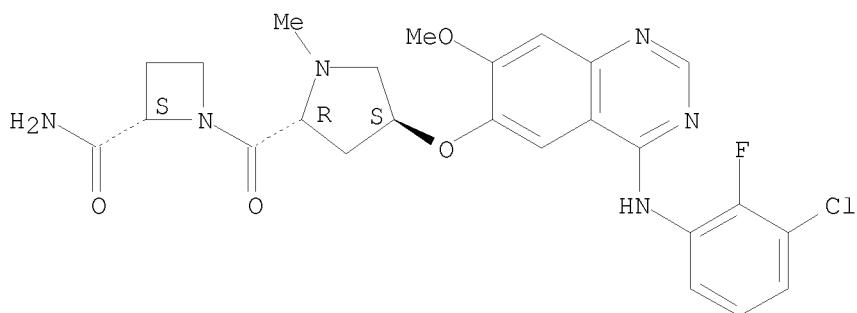
Absolute stereochemistry.



RN 849345-50-2 CAPLUS

CN 2-Azetidinecarboxamide, 1-[(2R,4S)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl]carbonyl]-, (2S)- (CA INDEX NAME)

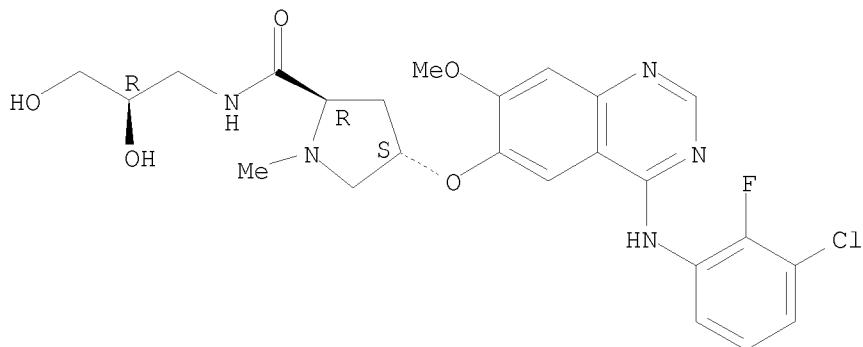
Absolute stereochemistry.



RN 849345-51-3 CAPLUS

CN 2-Pyrrolidinedicarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-[(2R)-2,3-dihydroxypropyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.

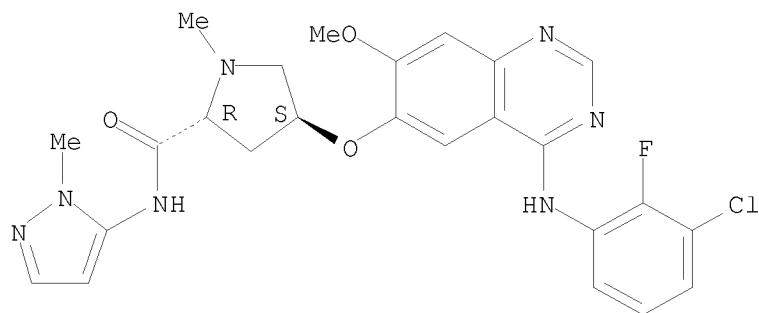


RN 849345-52-4 CAPLUS

CN 2-Pyrrolidinedicarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-N-(1-methyl-1H-pyrazol-5-yl)-, (2R,4S)- (CA INDEX NAME)

(INDEX NAME)

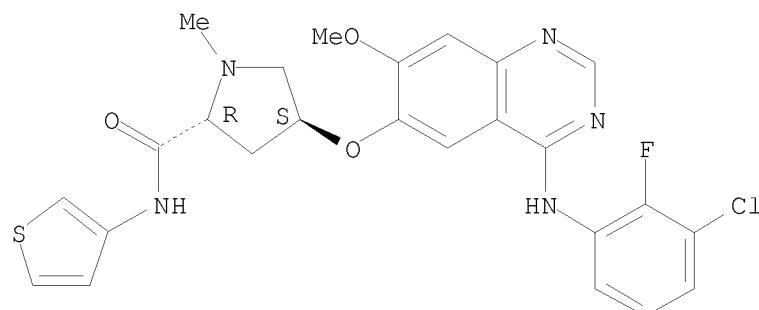
Absolute stereochemistry.



RN 849345-53-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, (2R,4S)- (CA INDEX NAME)

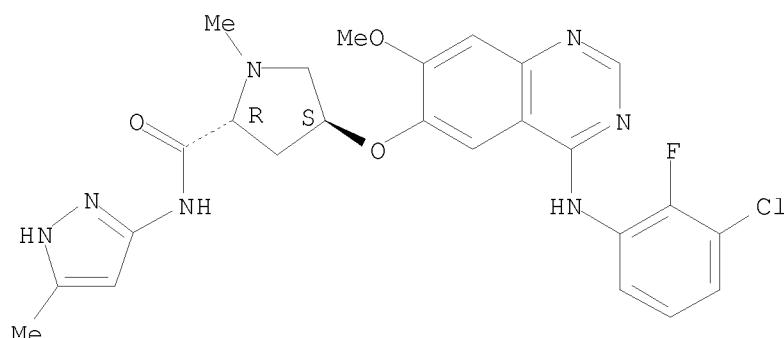
Absolute stereochemistry.



RN 849345-54-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-N-(5-methyl-1H-pyrazol-3-yl)-, (2R,4S)- (CA INDEX NAME)

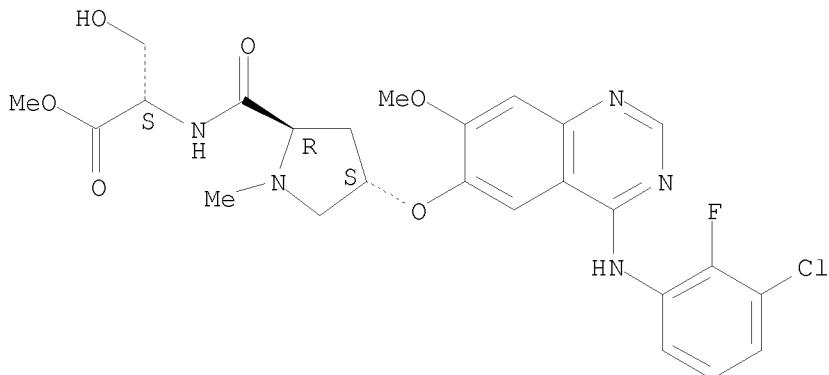
Absolute stereochemistry.



RN 849345-55-7 CAPLUS

CN L-Serine, (4S)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-D-prolyl-, methyl ester (9CI) (CA INDEX NAME)

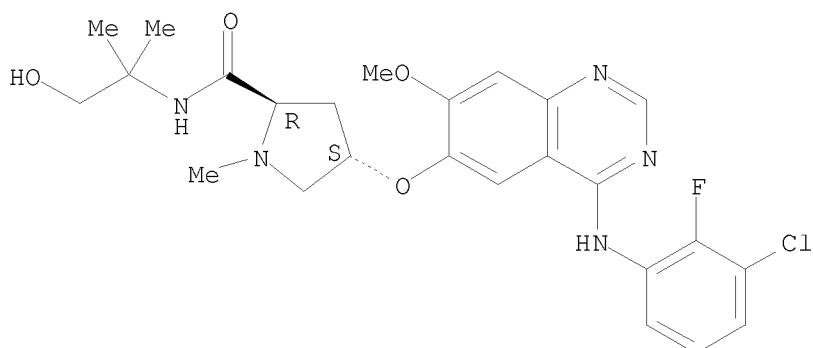
Absolute stereochemistry.



RN 849345-56-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(2-hydroxy-1,1-dimethylethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

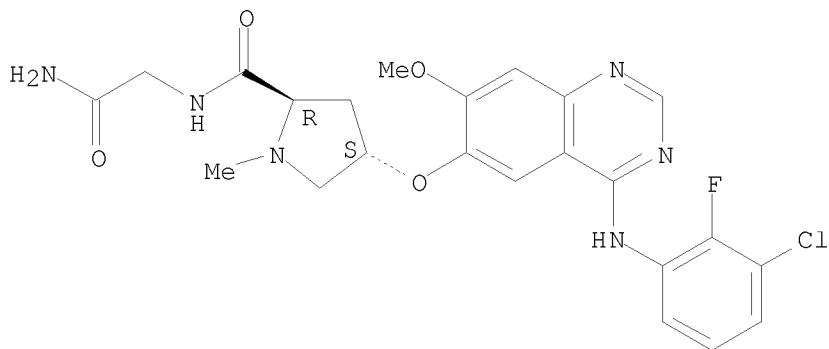
Absolute stereochemistry.



RN 849345-57-9 CAPLUS

CN Glycinamide, (4S)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-D-prolyl- (9CI) (CA INDEX NAME)

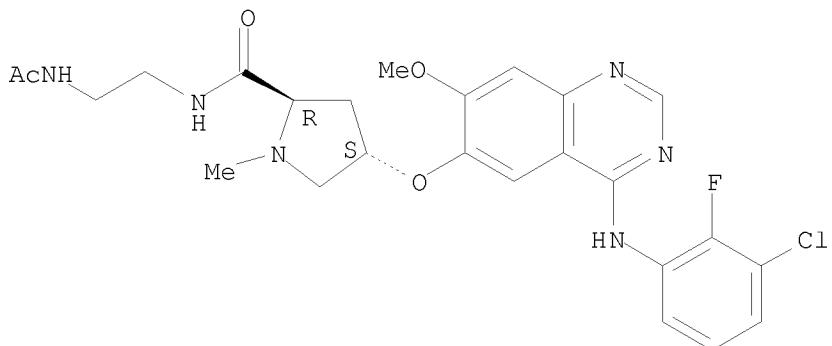
Absolute stereochemistry.



RN 849345-58-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, N-[2-(acetylamino)ethyl]-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (2R,4S)- (CA INDEX NAME)

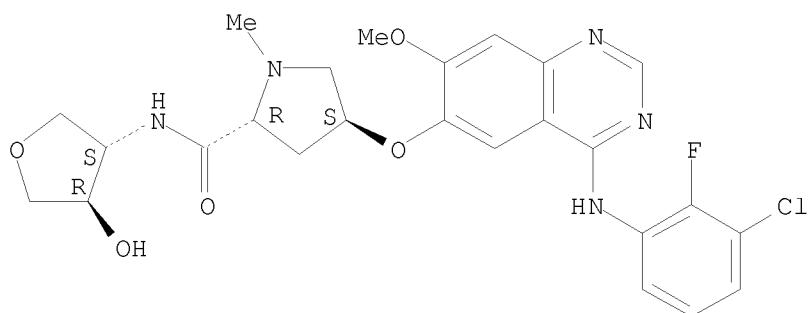
Absolute stereochemistry.



RN 849345-59-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-N-[(3S,4R)-tetrahydro-4-hydroxy-3-furanyl]-, (2R,4S)- (CA INDEX NAME)

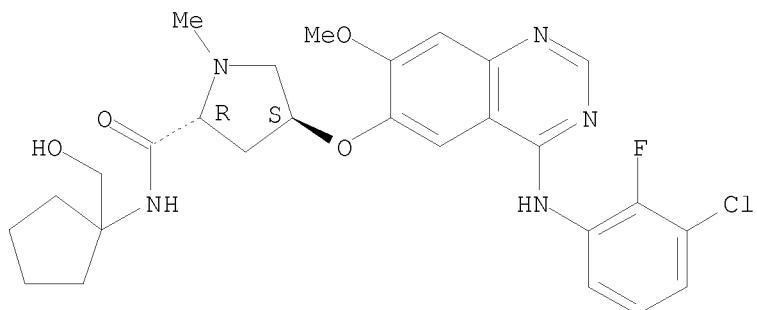
Absolute stereochemistry.



RN 849345-60-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-[1-(hydroxymethyl)cyclopentyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

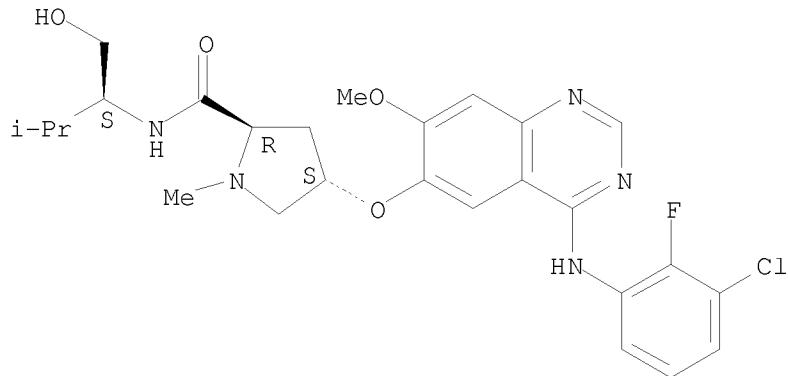
Absolute stereochemistry.



RN 849345-61-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[(1S)-1-(hydroxymethyl)-2-methylpropyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

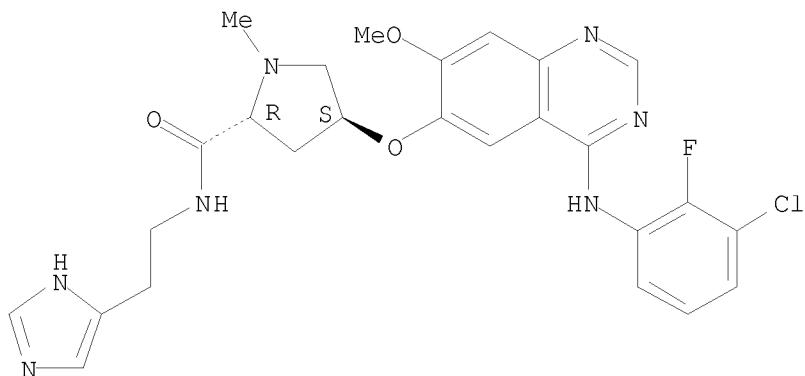
Absolute stereochemistry.



RN 849345-62-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[2-(1H-imidazol-5-yl)ethyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

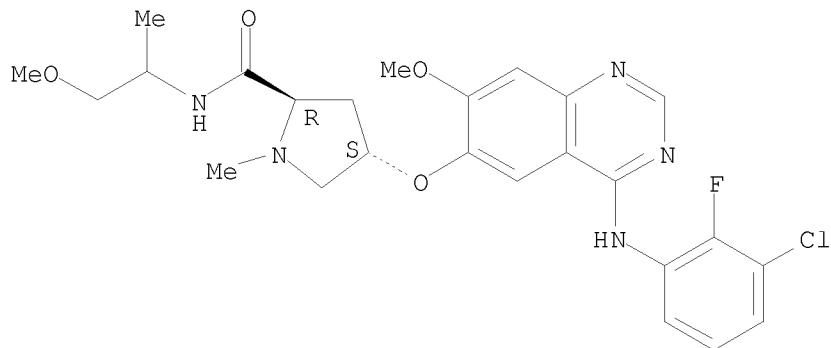
Absolute stereochemistry.



RN 849345-63-7 CAPLUS

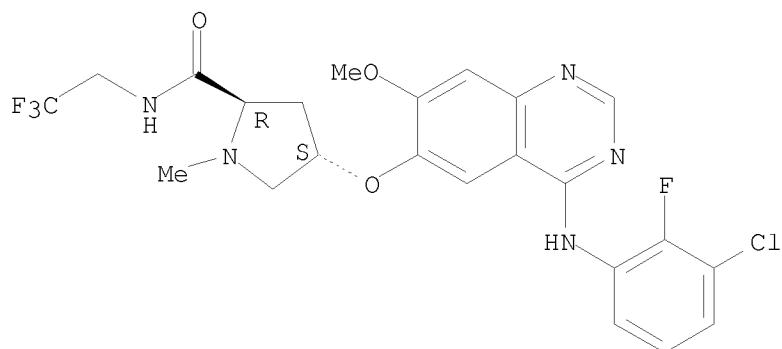
CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-(2-methoxy-1-methylethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



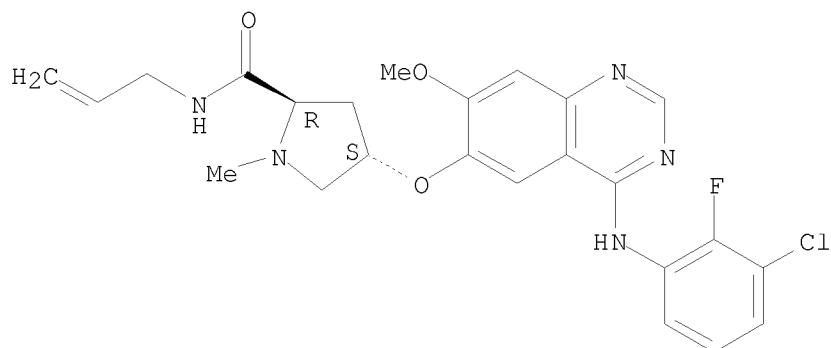
RN 849345-64-8 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-N-(2,2,2-trifluoroethyl)-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



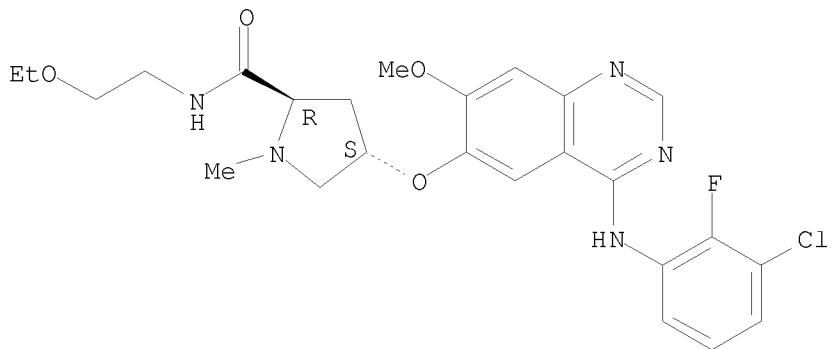
RN 849345-65-9 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-N-2-propen-1-yl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 849345-66-0 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(2-ethoxyethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

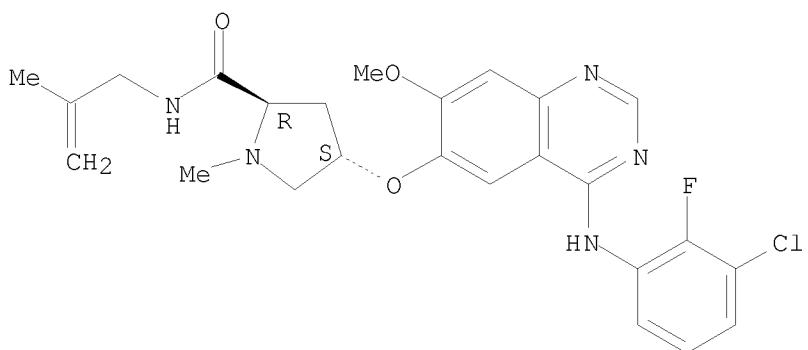
Absolute stereochemistry.



RN 849345-67-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, (2R,4S)- (CA INDEX NAME)

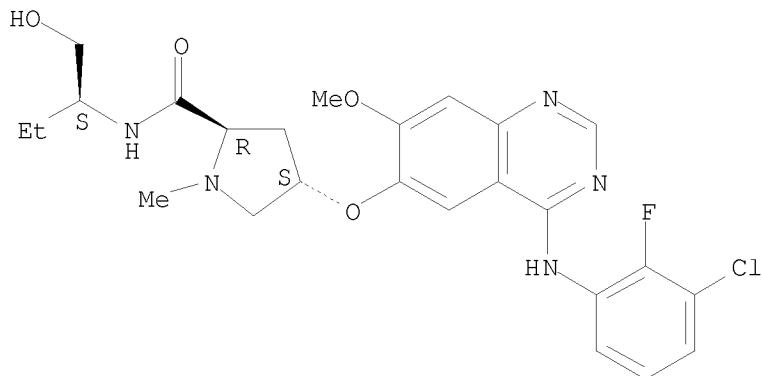
Absolute stereochemistry.



RN 849345-68-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-[(1S)-1-(hydroxymethyl)propyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

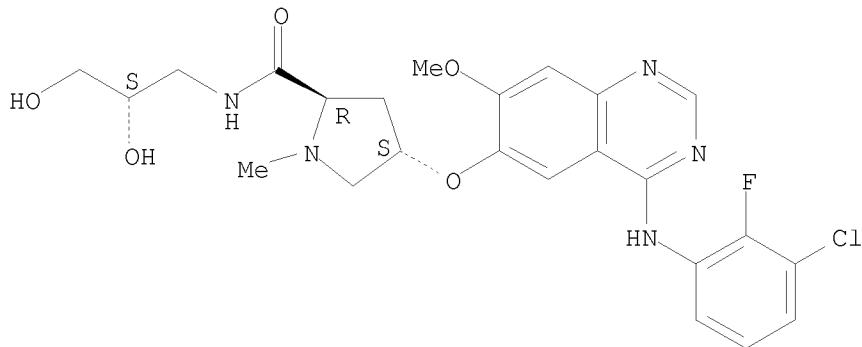
Absolute stereochemistry.



RN 849345-69-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[(2S)-2,3-dihydroxypropyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

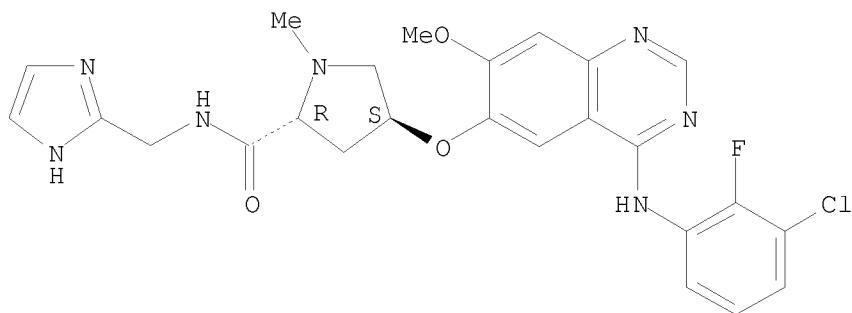
Absolute stereochemistry.



RN 849345-70-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-(1H-imidazol-2-ylmethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

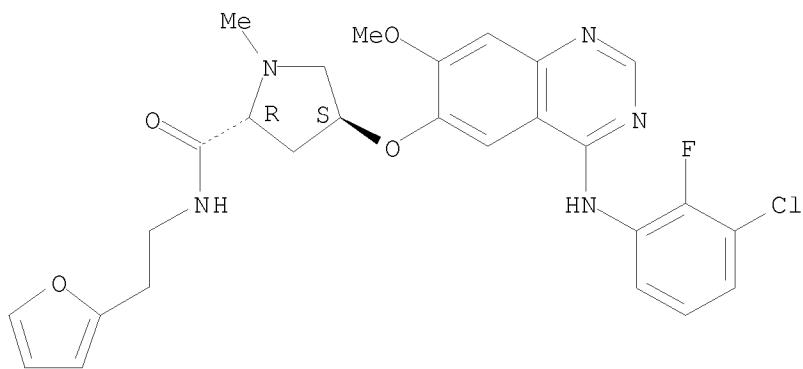
Absolute stereochemistry.



RN 849345-71-7 CAPLUS

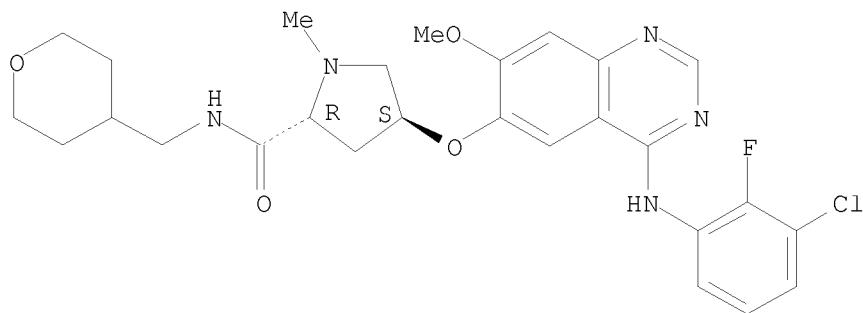
CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[2-(2-furanyl)ethyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



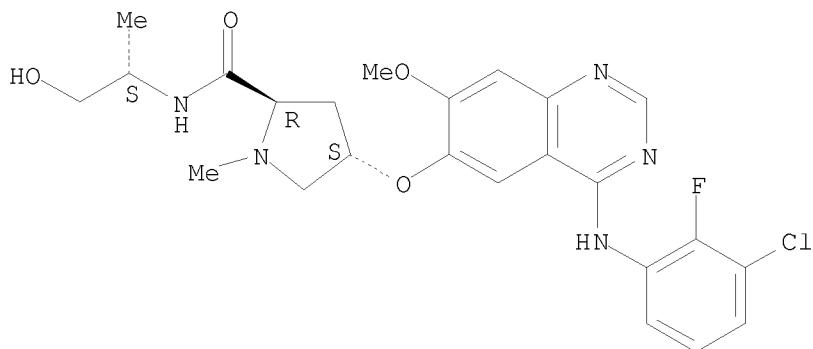
RN 849345-72-8 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-N-[tetrahydro-2H-pyran-4-yl)methyl]-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 849345-73-9 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-[(1S)-2-hydroxy-1-methylethyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

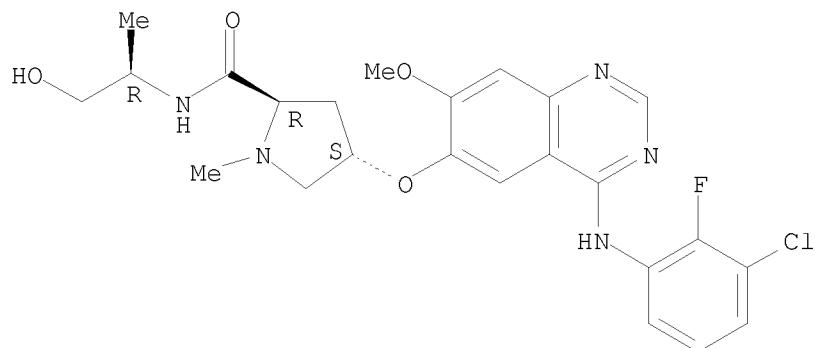
Absolute stereochemistry.



RN 849345-74-0 CAPLUS
 CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-[(1R)-2-hydroxy-1-methylethyl]-1-methyl-, (2R,4S)-

(CA INDEX NAME)

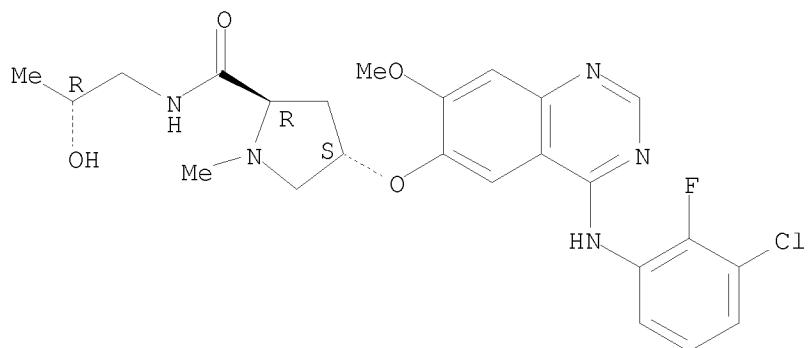
Absolute stereochemistry.



RN 849345-75-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-[(2R)-2-hydroxypropyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

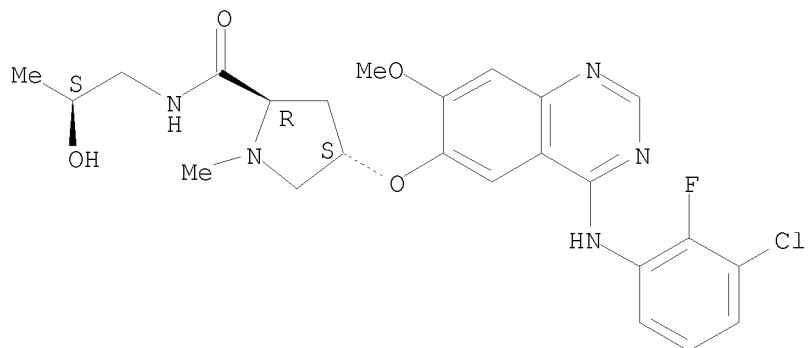
Absolute stereochemistry.



RN 849345-76-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-[(2S)-2-hydroxypropyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

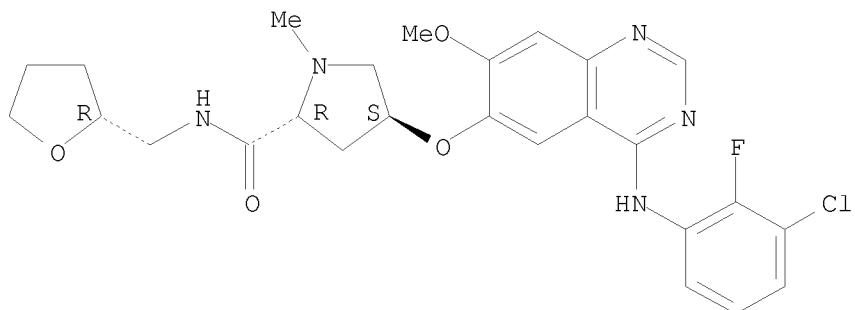
Absolute stereochemistry.



RN 849345-77-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-N-[(2R)-tetrahydro-2-furanyl]methyl]-, (2R,4S)- (CA INDEX NAME)

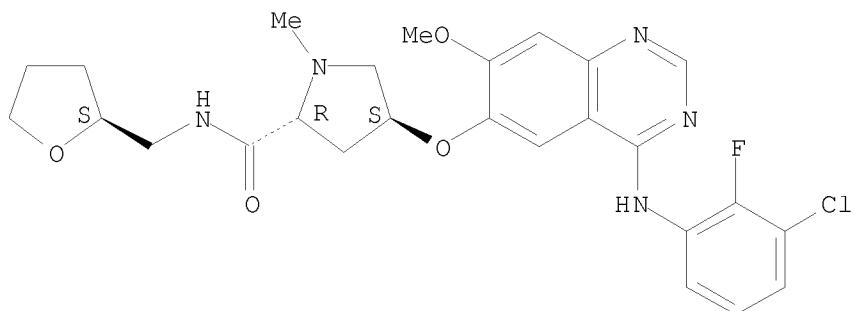
Absolute stereochemistry.



RN 849345-78-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-N-[(2S)-tetrahydro-2-furanyl]methyl]-, (2R,4S)- (CA INDEX NAME)

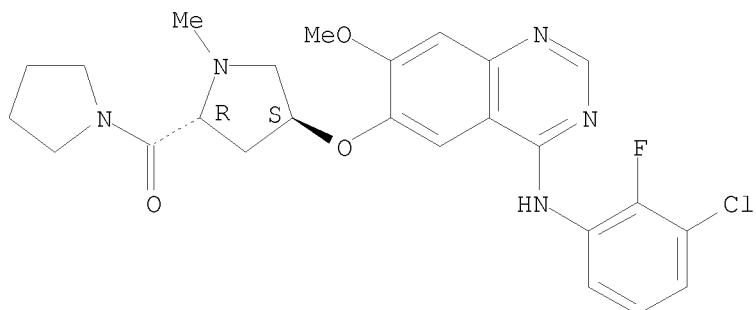
Absolute stereochemistry.



RN 849345-79-5 CAPLUS

CN Methanone, [(2R,4S)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-2-pyrrolidinyl]-1-pyrrolidinyl- (CA INDEX NAME)

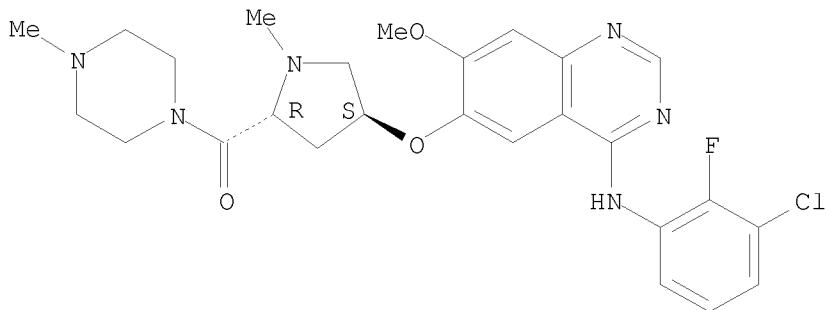
Absolute stereochemistry.



RN 849345-80-8 CAPLUS

CN Methanone, [(2R,4S)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl](4-methyl-1-piperazinyl)- (CA INDEX NAME)

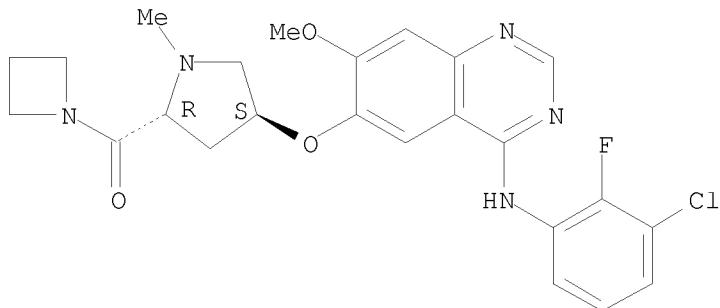
Absolute stereochemistry.



RN 849345-81-9 CAPLUS

CN Methanone, 1-azetidinyl[(2R,4S)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl]- (CA INDEX NAME)

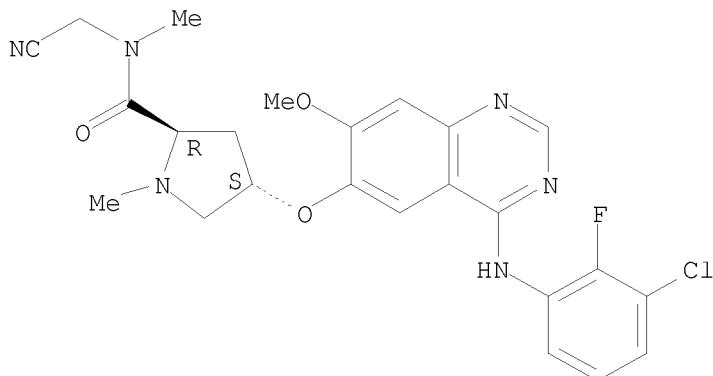
Absolute stereochemistry.



RN 849345-82-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(cyanomethyl)-N,1-dimethyl-, (2R,4S)- (CA INDEX NAME)

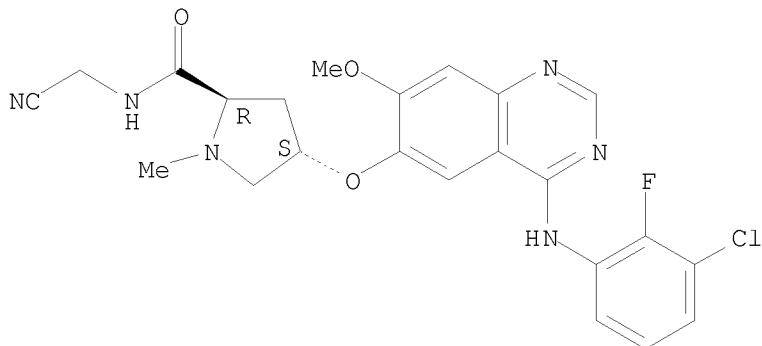
Absolute stereochemistry.



RN 849345-83-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-(cyanomethyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

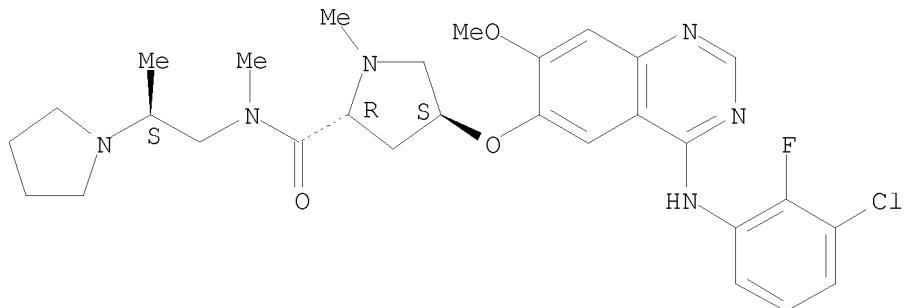
Absolute stereochemistry.



RN 849345-84-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,1-dimethyl-N-[(2S)-2-(1-pyrrolidinyl)propyl]-, (2R,4S)- (CA INDEX NAME)

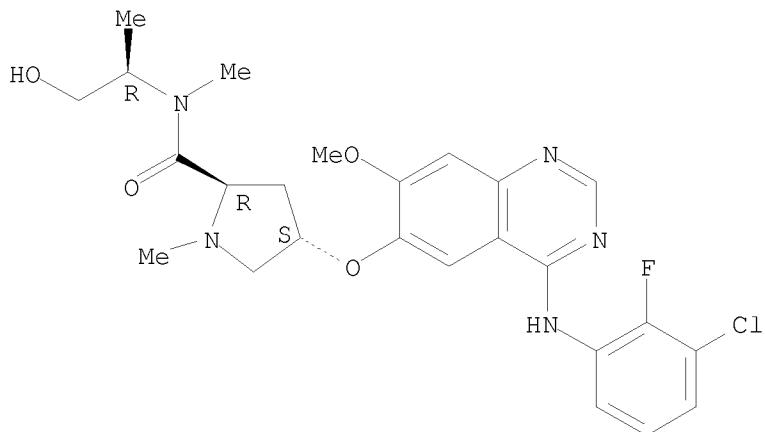
Absolute stereochemistry.



RN 849345-85-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[(1R)-2-hydroxy-1-methylethyl]-N,1-dimethyl-, (2R,4S)- (CA INDEX NAME)

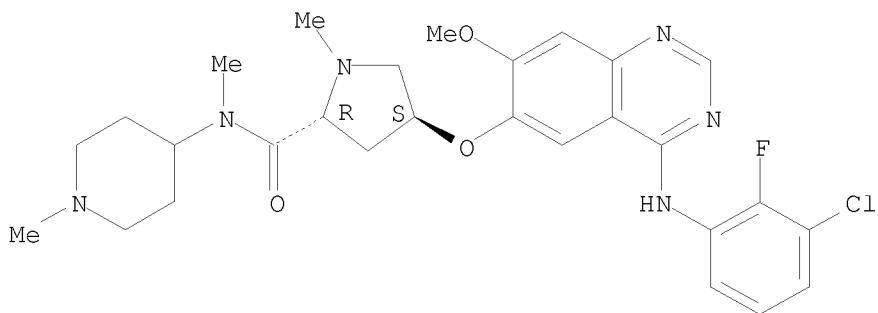
Absolute stereochemistry.



RN 849345-86-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,1-dimethyl-N-(1-methyl-4-piperidinyl)-, (2R,4S)-
(CA INDEX NAME)

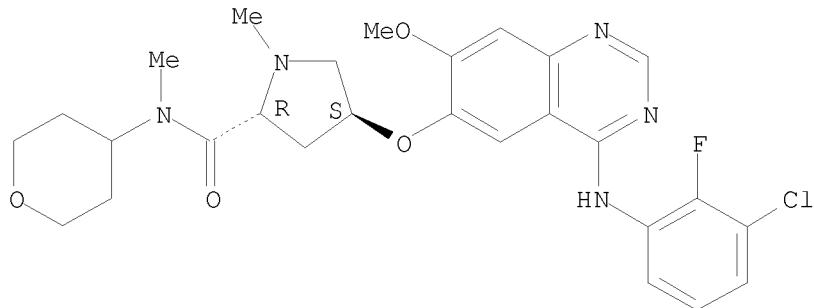
Absolute stereochemistry.



RN 849345-87-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,1-dimethyl-N-(tetrahydro-2H-pyran-4-yl)-, (2R,4S)-
(CA INDEX NAME)

Absolute stereochemistry.

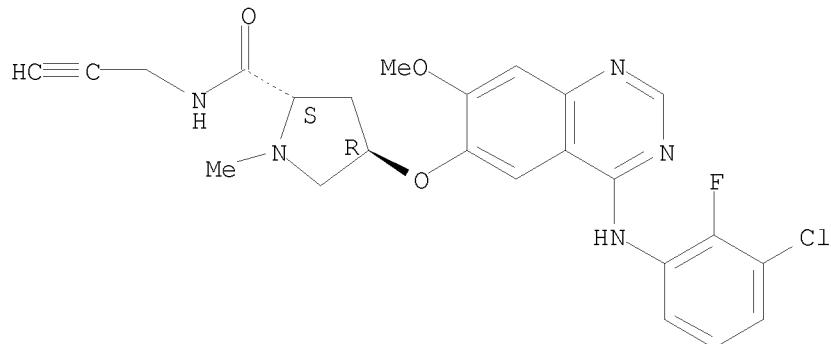


RN 849345-93-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-

6-quinazolinyl]oxy]-1-methyl-N-2-propyn-1-yl-, (2S,4R)- (CA INDEX NAME)

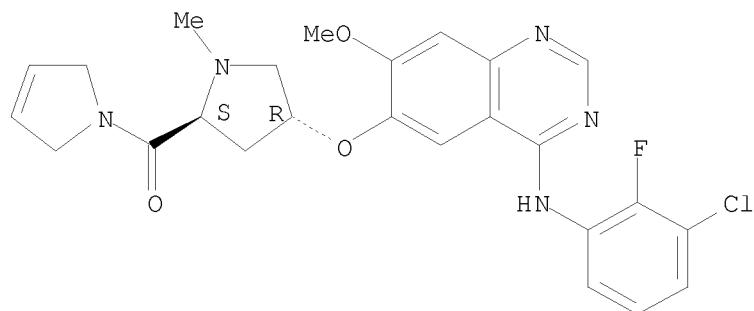
Absolute stereochemistry.



RN 849345-94-4 CAPLUS

CN Methanone, [(2S,4R)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl](2,5-dihydro-1H-pyrrol-1-yl)-(CA INDEX NAME)

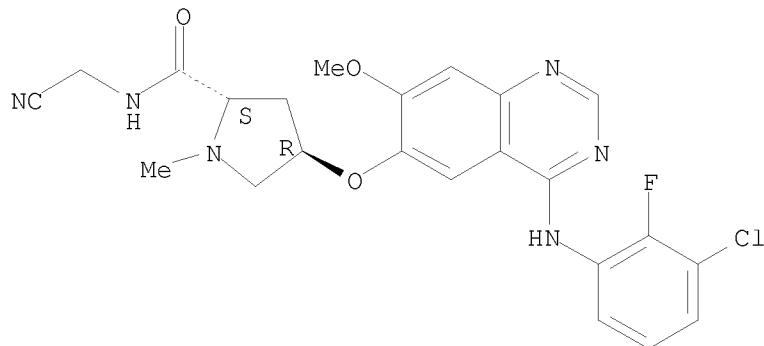
Absolute stereochemistry.



RN 849345-95-5 CAPLUS

CN 2-Pyrrolidinylcarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(cyanomethyl)-1-methyl-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.

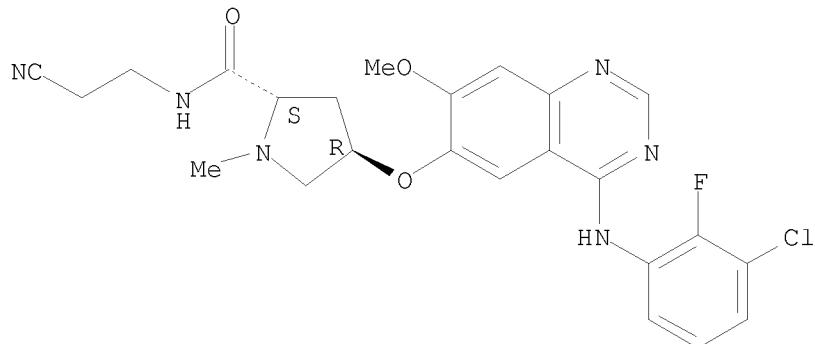


RN 849345-96-6 CAPLUS

CN 2-Pyrrolidinylcarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-

6-quinazolinyl]oxy]-N-(2-cyanoethyl)-1-methyl-, (2S,4R)- (CA INDEX NAME)

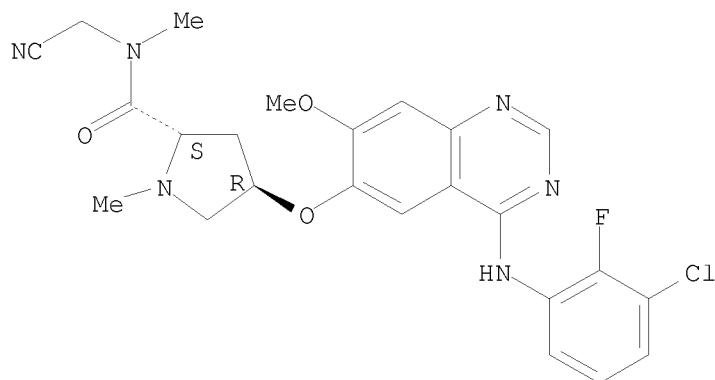
Absolute stereochemistry.



RN 849345-97-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(cyanomethyl)-1-dimethyl-, (2S,4R)- (CA INDEX NAME)

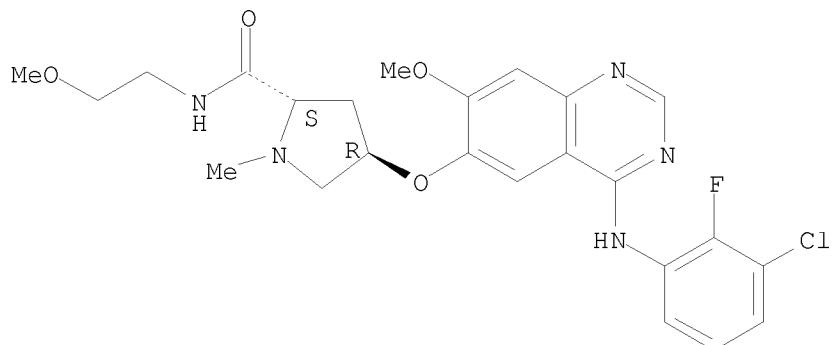
Absolute stereochemistry.



RN 849345-98-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(2-methoxyethyl)-1-methyl-, (2S,4R)- (CA INDEX NAME)

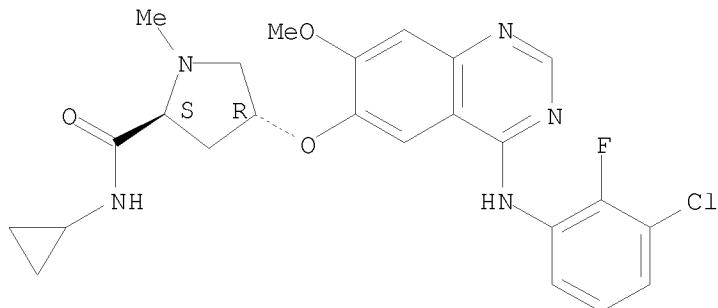
Absolute stereochemistry.



RN 849345-99-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-cyclopropyl-1-methyl-, (2S,4R)- (CA INDEX NAME)

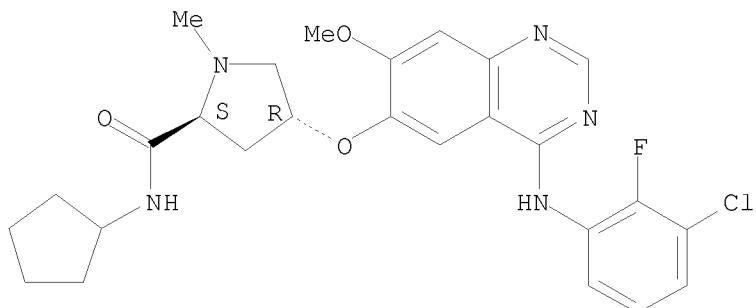
Absolute stereochemistry.



RN 849346-00-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-cyclopentyl-1-methyl-, (2S,4R)- (CA INDEX NAME)

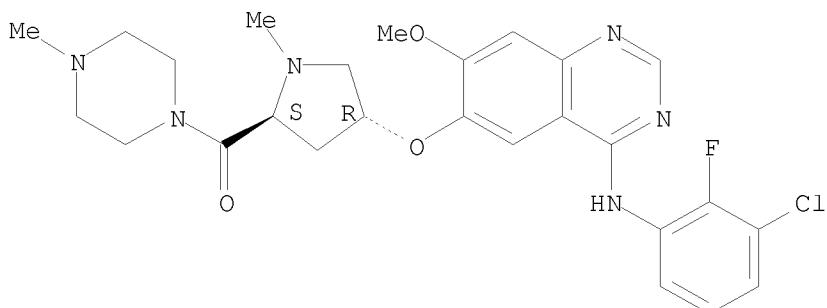
Absolute stereochemistry.



RN 849346-01-6 CAPLUS

CN Methanone, [(2S,4R)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-2-pyrrolidinyl](4-methyl-1-piperazinyl)- (CA INDEX NAME)

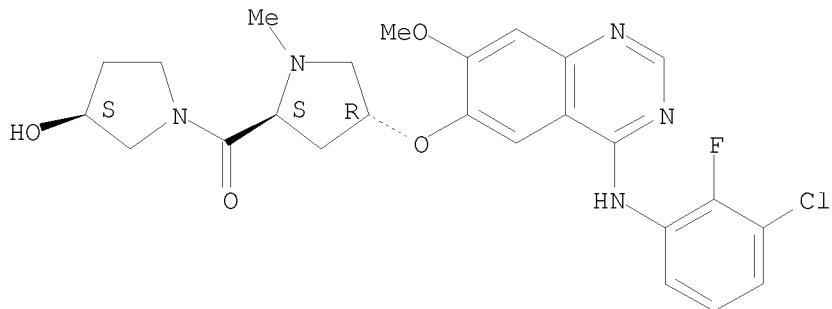
Absolute stereochemistry.



RN 849346-02-7 CAPLUS

CN Methanone, [(2S,4R)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-2-pyrrolidinyl][(3S)-3-hydroxy-1-pyrrolidinyl]- (CA INDEX NAME)

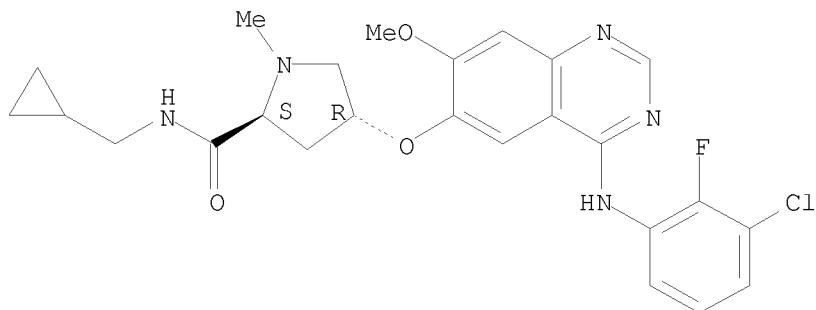
Absolute stereochemistry.



RN 849346-03-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(cyclopropylmethyl)-1-methyl-, (2S,4R)- (CA INDEX NAME)

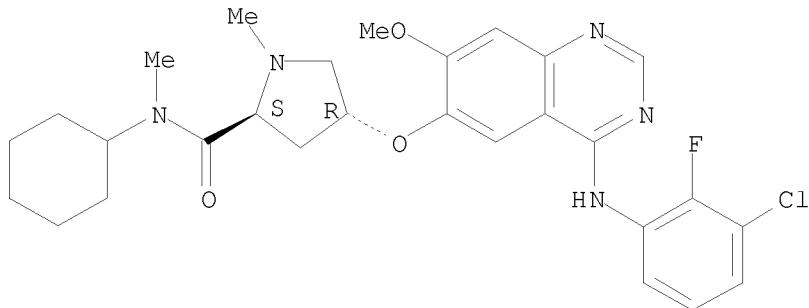
Absolute stereochemistry.



RN 849346-04-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-cyclohexyl-N,1-dimethyl-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.

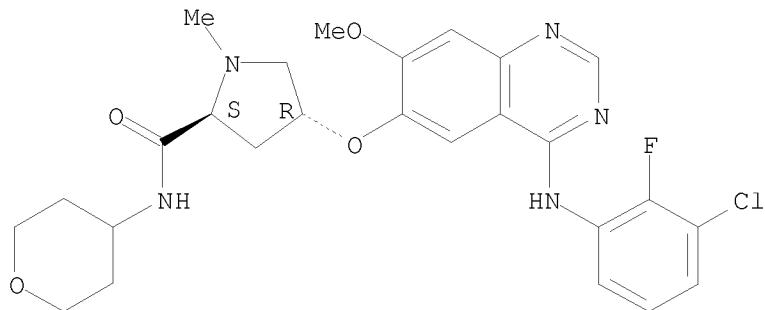


RN 849346-05-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-

6-quinazolinyl]oxy]-1-methyl-N-(tetrahydro-2H-pyran-4-yl)-, (2*S*,4*R*)- (CA INDEX NAME)

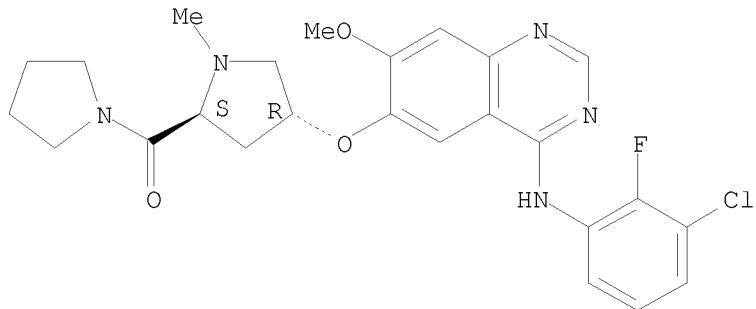
Absolute stereochemistry.



RN 849346-06-1 CAPLUS

CN Methanone, [(2S,4R)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl]-1-pyrrolidinyl- (CA INDEX NAME)

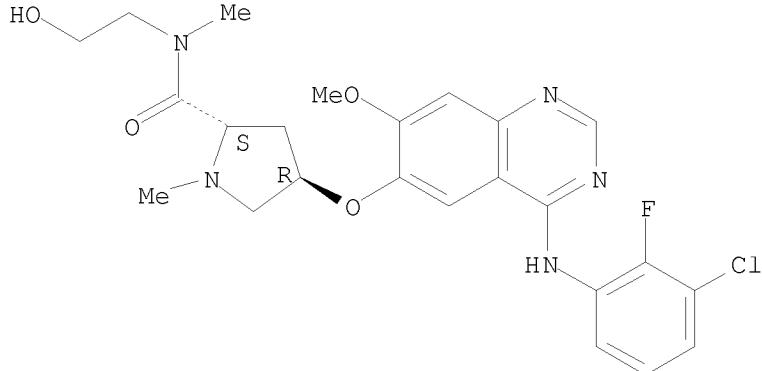
Absolute stereochemistry.



RN 849346-07-2 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(2-hydroxyethyl)-N,1-dimethyl-, (2S,4R)- (CA INDEX NAME)

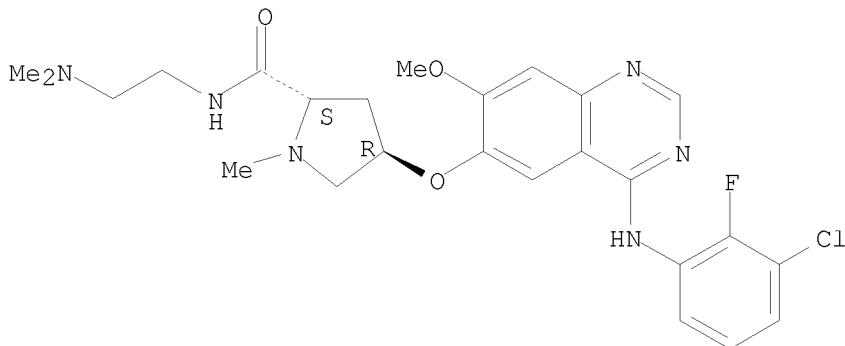
Absolute stereochemistry.



RN 849346-08-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-[2-(dimethylamino)ethyl]-1-methyl-, (2S,4R)- (CA INDEX NAME)

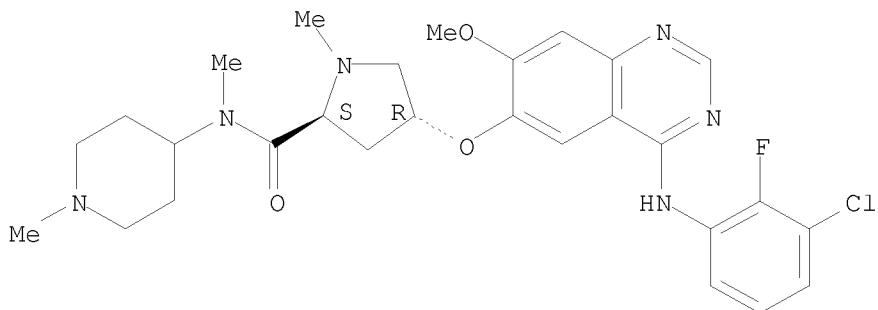
Absolute stereochemistry.



RN 849346-09-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,1-dimethyl-N-(1-methyl-4-piperidinyl)-, (2S,4R)- (CA INDEX NAME)

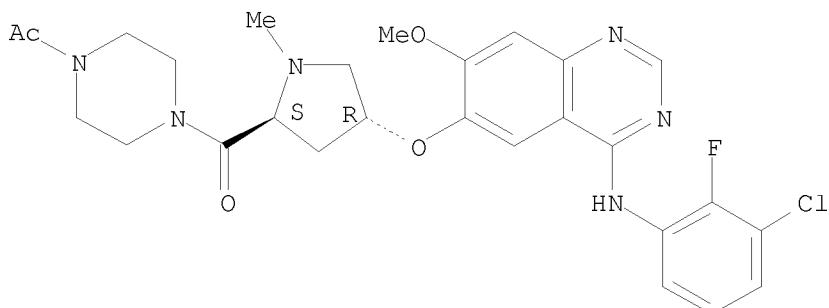
Absolute stereochemistry.



RN 849346-10-7 CAPLUS

CN Ethanone, 1-[4-[(2S,4R)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-1-methyl-2-pyrrolidinyl]carbonyl]-1-piperazinyl- (CA INDEX NAME)

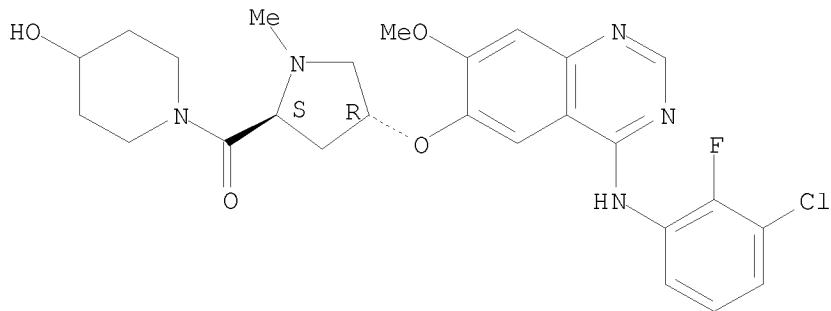
Absolute stereochemistry.



RN 849346-11-8 CAPLUS

CN Methanone, [(2S,4R)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl](4-hydroxy-1-piperidinyl)- (CA INDEX NAME)

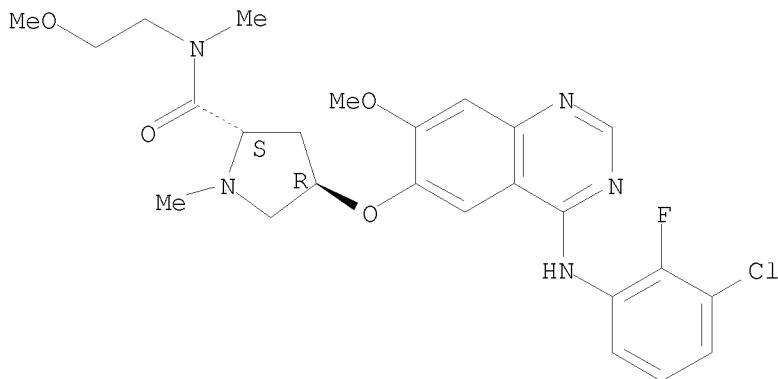
Absolute stereochemistry.



RN 849346-12-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(2-methoxyethyl)-N,1-dimethyl-, (2S,4R)- (CA INDEX NAME)

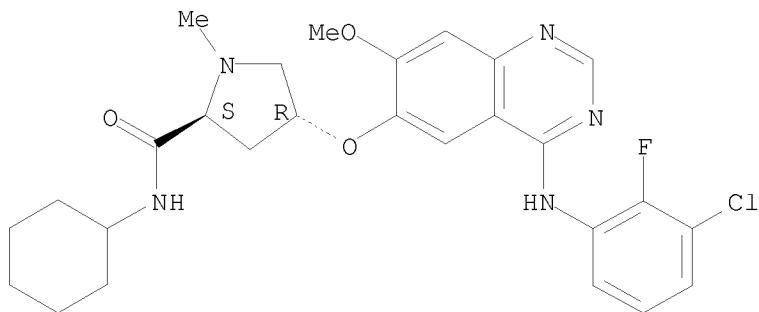
Absolute stereochemistry.



RN 849346-13-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-cyclohexyl-1-methyl-, (2S,4R)- (CA INDEX NAME)

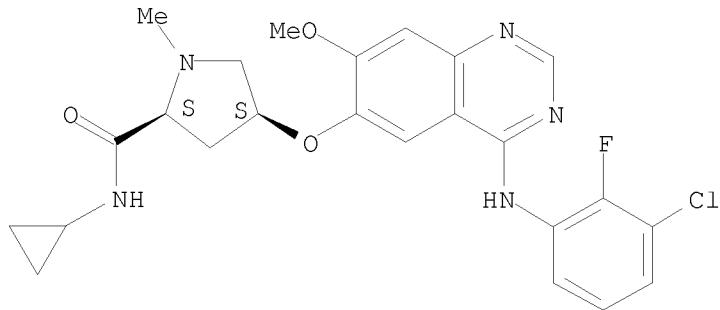
Absolute stereochemistry.



RN 849346-18-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-cyclopropyl-1-methyl-, (2S,4S)- (CA INDEX NAME)

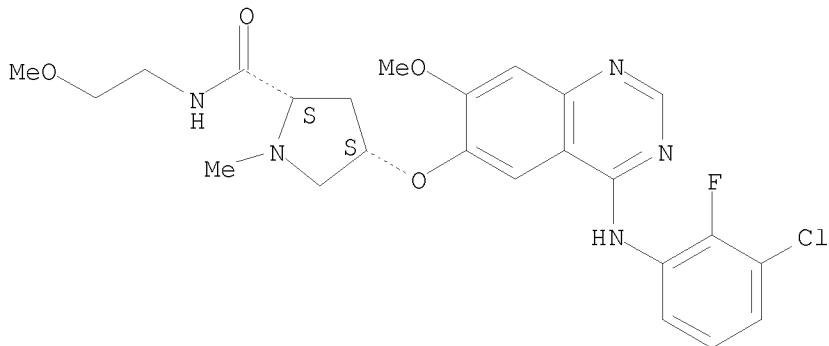
Absolute stereochemistry.



RN 849346-19-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(2-methoxyethyl)-1-methyl-, (2S,4S)- (CA INDEX NAME)

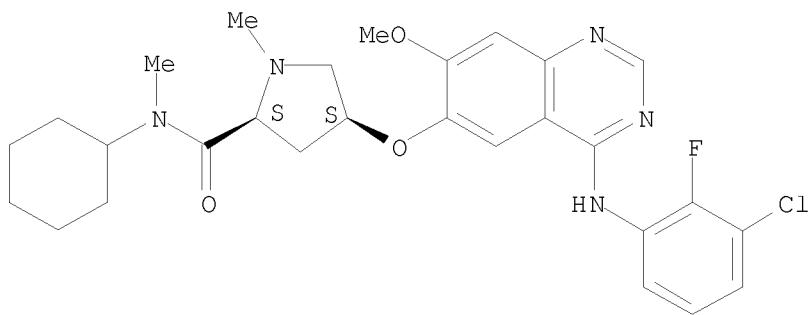
Absolute stereochemistry.



RN 849346-20-9 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-cyclohexyl-N,1-dimethyl-, (2S,4S)- (CA INDEX NAME)

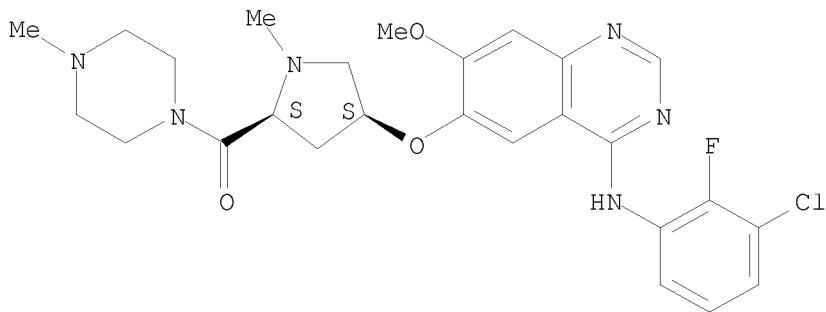
Absolute stereochemistry.



RN 849346-21-0 CAPLUS

CN Methanone, [(2S,4S)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-2-pyrrolidinyl](4-methyl-1-piperazinyl)- (CA INDEX NAME)

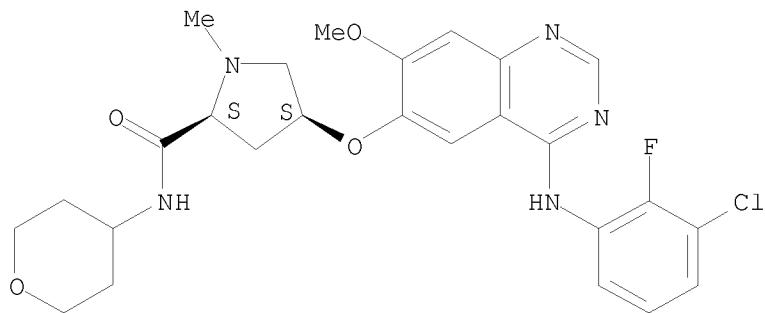
Absolute stereochemistry.



RN 849346-22-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-N-(tetrahydro-2H-pyran-4-yl)-, (2S,4S)- (CA INDEX NAME)

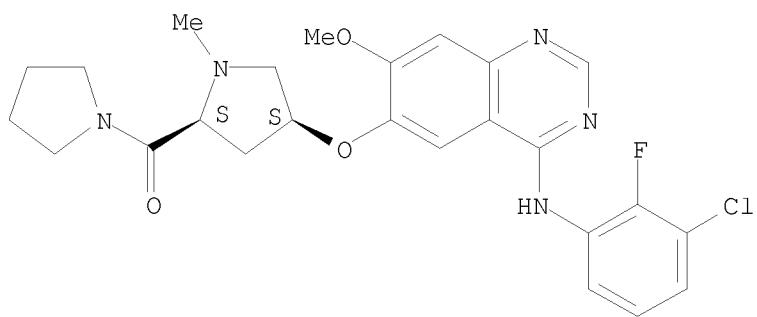
Absolute stereochemistry.



RN 849346-23-2 CAPLUS

CN Methanone, [(2S,4S)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-2-pyrrolidinyl]-1-pyrrolidinyl- (CA INDEX NAME)

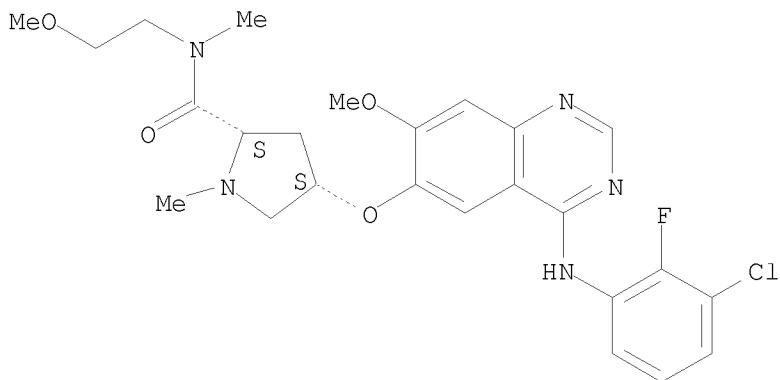
Absolute stereochemistry.



RN 849346-24-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-(2-methoxyethyl)-N,1-dimethyl-, (2S,4S)- (CA INDEX NAME)

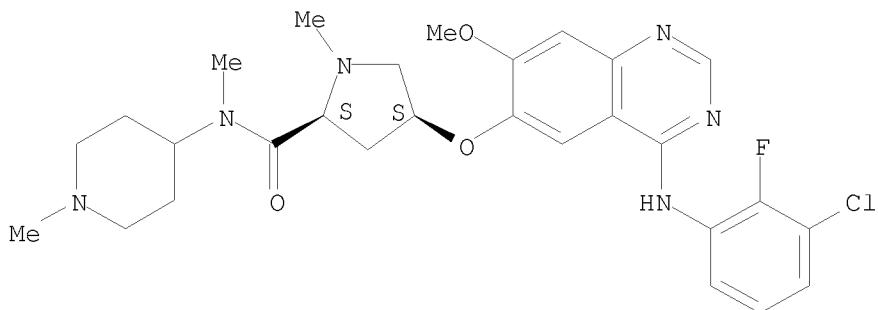
Absolute stereochemistry.



RN 849346-25-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,1-dimethyl-N-(1-methyl-4-piperidinyl)-, (2S,4S)- (CA INDEX NAME)

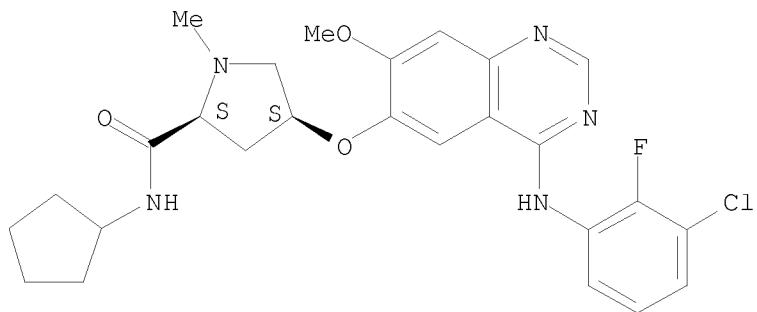
Absolute stereochemistry.



RN 849346-26-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N-cyclopentyl-1-methyl-, (2S,4S)- (CA INDEX NAME)

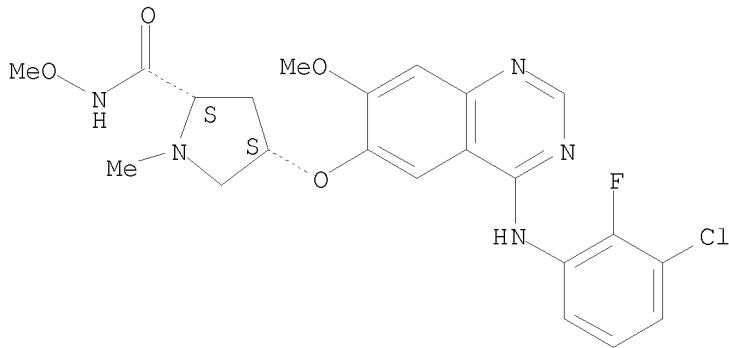
Absolute stereochemistry.



RN 849346-27-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-methoxy-1-methyl-, (2S,4S)- (CA INDEX NAME)

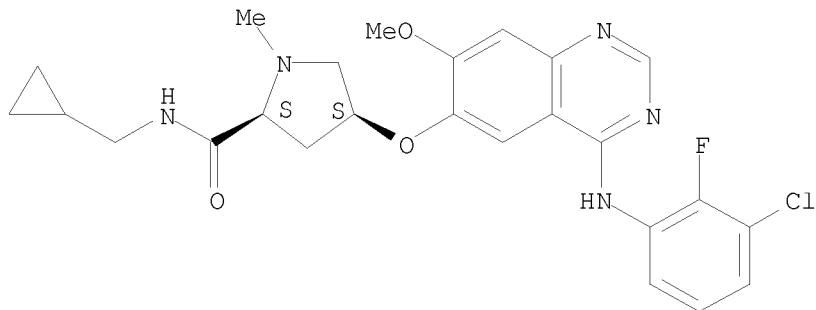
Absolute stereochemistry.



RN 849346-28-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(cyclopropylmethyl)-1-methyl-, (2S,4S)- (CA INDEX NAME)

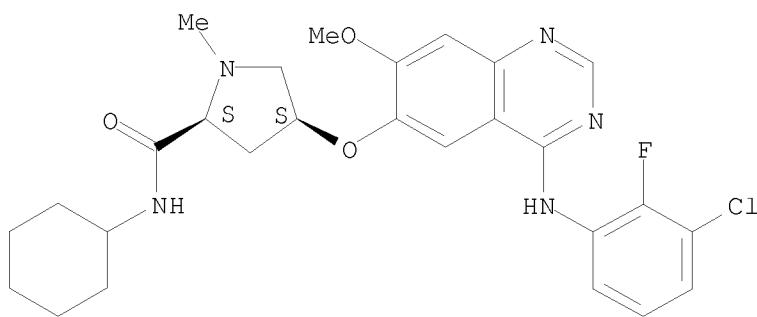
Absolute stereochemistry.



RN 849346-29-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-cyclohexyl-1-methyl-, (2S,4S)- (CA INDEX NAME)

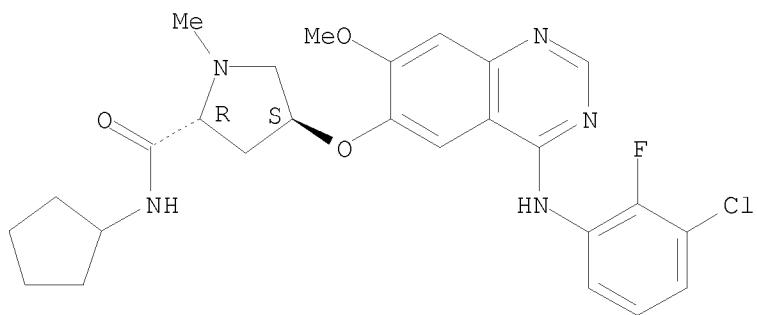
Absolute stereochemistry.



RN 849346-30-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(cyclopentylmethyl)-, (2R,4S)- (CA INDEX NAME)

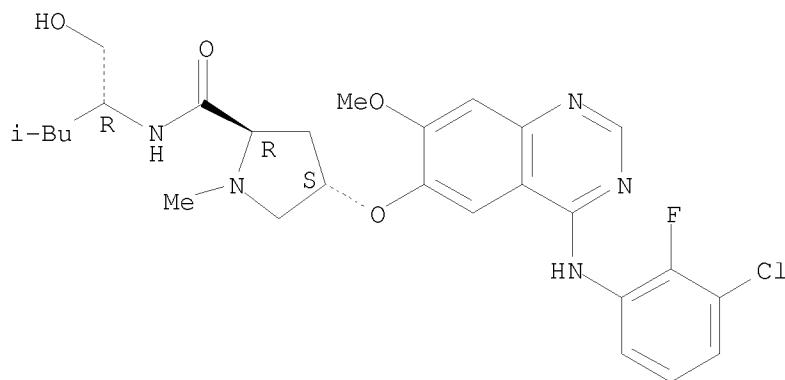
Absolute stereochemistry.



RN 849346-32-3 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-[1R)-1-(hydroxymethyl)-3-methylbutyl]-1-methyl-, (2R,4S)- (CA INDEX NAME)

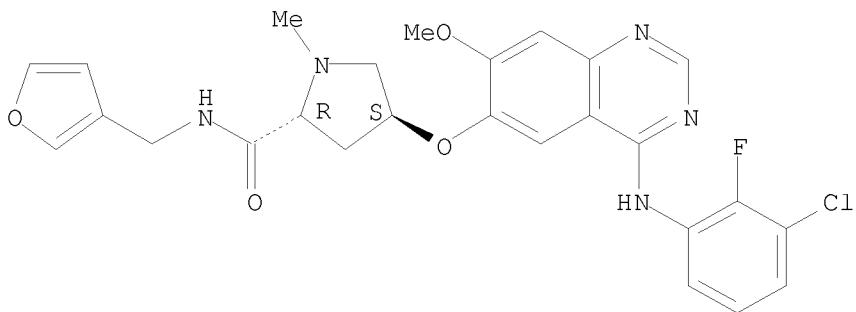
Absolute stereochemistry.



RN 849346-33-4 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N-(3-furanyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

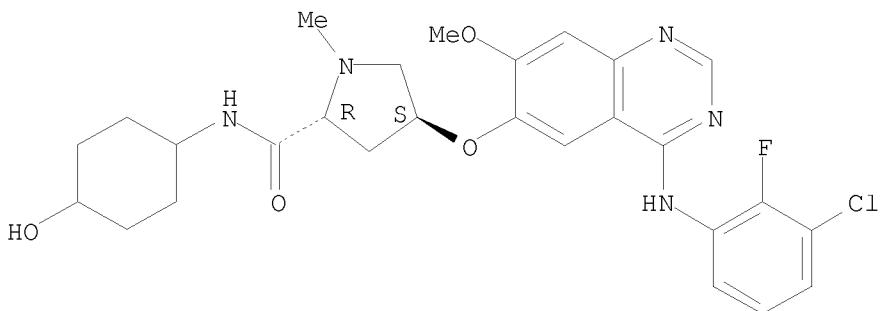
Absolute stereochemistry.



RN 849419-45-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N-(4-hydroxycyclohexyl)-1-methyl-, (2R,4S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 849344-98-5P 849344-99-6P 849345-00-2P

849345-12-6P 849345-13-7P 849345-14-8P

849345-90-0P 849345-91-1P 849345-92-2P

849346-15-2P 849346-16-3P 849346-17-4P

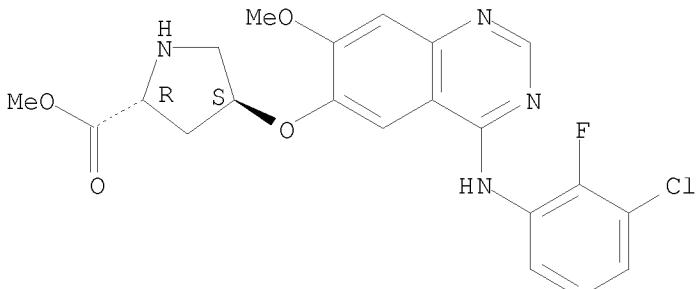
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of proline quinazoline derivs. as antiproliferative agents)

RN 849344-98-5 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, methyl ester, (4S)- (CA INDEX NAME)

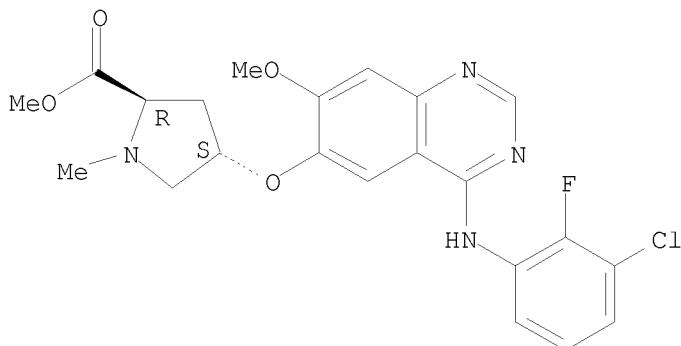
Absolute stereochemistry.



RN 849344-99-6 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4S)- (CA INDEX NAME)

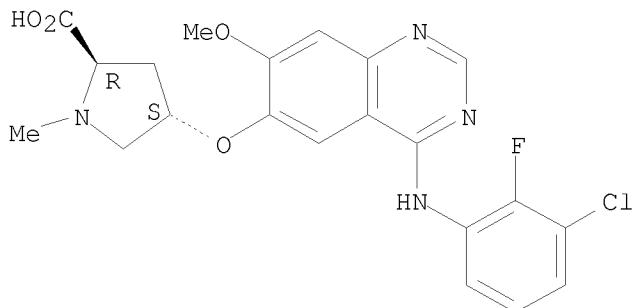
Absolute stereochemistry.



RN 849345-00-2 CAPLUS

CN D-Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4S)- (CA INDEX NAME)

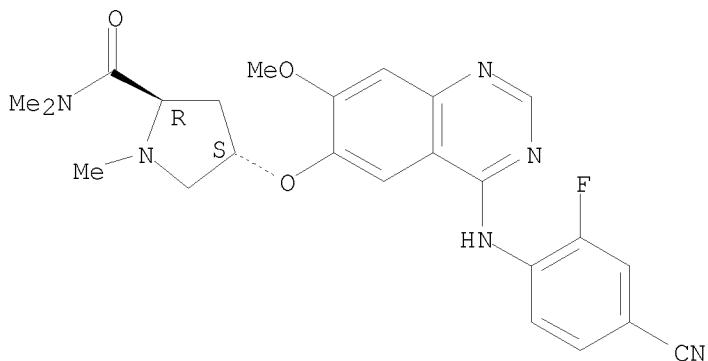
Absolute stereochemistry.



RN 849345-12-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(4-cyano-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

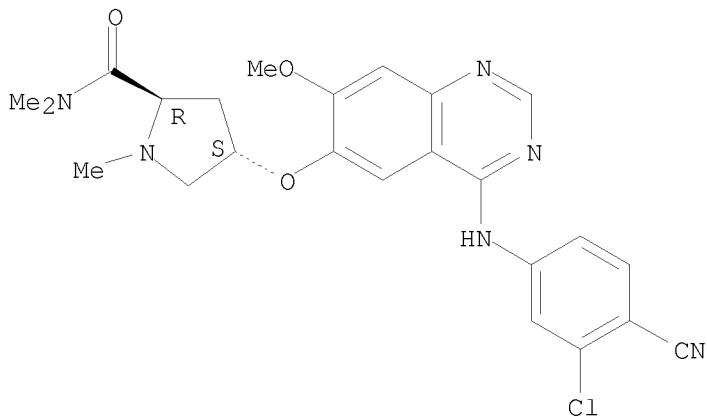
Absolute stereochemistry.



RN 849345-13-7 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-4-cyanophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

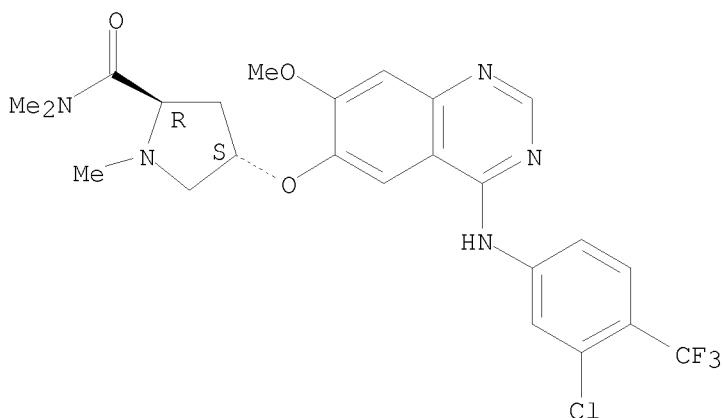
Absolute stereochemistry.



RN 849345-14-8 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-4-(trifluoromethyl)phenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N,1-trimethyl-, (2R,4S)- (CA INDEX NAME)

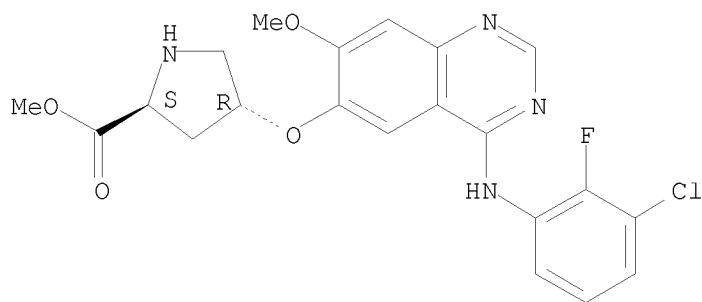
Absolute stereochemistry.



RN 849345-90-0 CAPLUS

CN L-Proline, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-, methyl ester, monohydrochloride, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

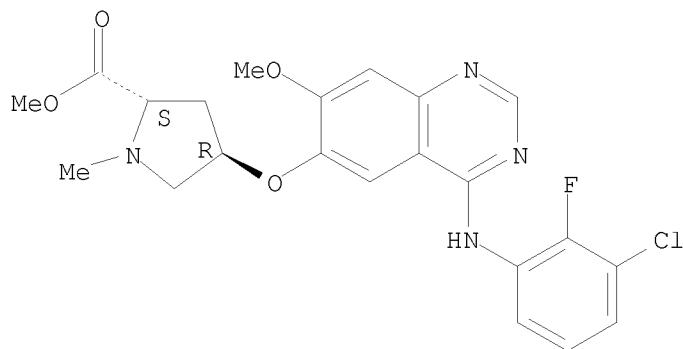


● HCl

RN 849345-91-1 CAPLUS

CN L-Proline, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, methyl ester, (4R)- (CA INDEX NAME)

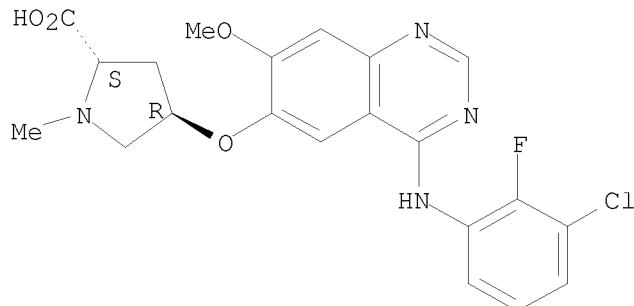
Absolute stereochemistry.



RN 849345-92-2 CAPLUS

CN L-Proline, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, (4R)- (CA INDEX NAME)

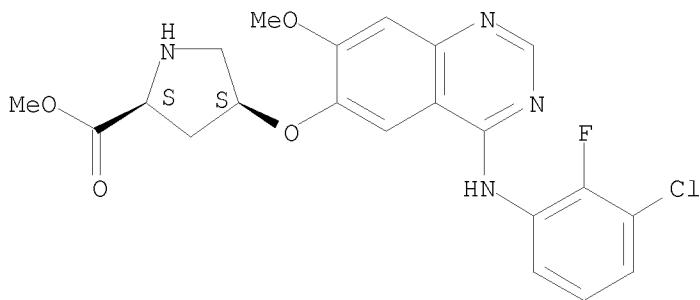
Absolute stereochemistry.



RN 849346-15-2 CAPLUS

CN L-Proline, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-, methyl ester, (4S)- (CA INDEX NAME)

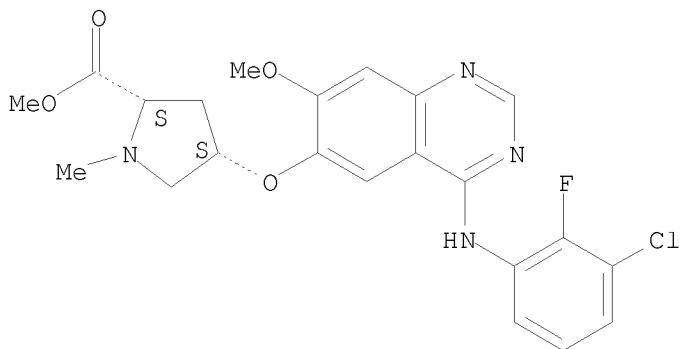
Absolute stereochemistry.



RN 849346-16-3 CAPLUS

CN L-Proline, 4-[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, methyl ester, (4S)- (CA INDEX NAME)

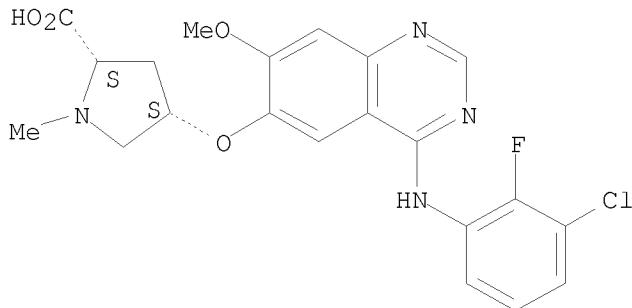
Absolute stereochemistry.



RN 849346-17-4 CAPLUS

CN L-Proline, 4-[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

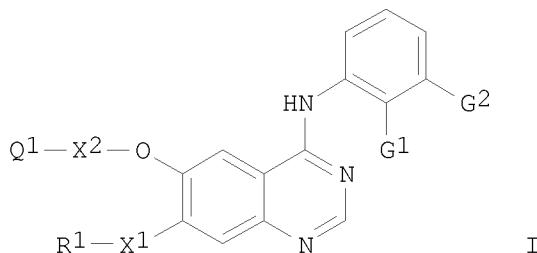
THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2003:796670 CAPLUS

DOCUMENT NUMBER: 139:307787
 TITLE: Preparation of 4-anilinoquinazolines as antiproliferative agents
 INVENTOR(S): Bradbury, Robert Hugh; Hennequin, Laurent Francois Andre; Kettle, Jason Grant
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
 SOURCE: PCT Int. Appl., 190 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------------|------------------|----------|
| WO 2003082831 | A1 | 20031009 | WO 2003-GB1306 | 20030326 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2479642 | A1 | 20031009 | CA 2003-2479642 | 20030326 |
| AU 2003214443 | A1 | 20031013 | AU 2003-214443 | 20030326 |
| EP 1487806 | A1 | 20041222 | EP 2003-710015 | 20030326 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003008670 | A | 20050201 | BR 2003-8670 | 20030326 |
| CN 1656081 | A | 20050817 | CN 2003-811739 | 20030326 |
| JP 2005529092 | T | 20050929 | JP 2003-580299 | 20030326 |
| JP 3891493 | B2 | 20070314 | | |
| CN 101003515 | A | 20070725 | CN 2007-10004468 | 20030326 |
| NZ 535014 | A | 20070727 | NZ 2003-535014 | 20030326 |
| RU 2345989 | C2 | 20090210 | RU 2004-131683 | 20030326 |
| US 20050215574 | A1 | 20050929 | US 2004-508675 | 20040922 |
| MX 2004009486 | A | 20050125 | MX 2004-9486 | 20040928 |
| NO 2004004325 | A | 20041216 | NO 2004-4325 | 20041012 |
| JP 2006249093 | A | 20060921 | JP 2006-102765 | 20060404 |
| US 20080269487 | A1 | 20081030 | US 2008-147250 | 20080626 |
| PRIORITY APPLN. INFO.: | | | | |
| | | GB 2002-7323 | A | 20020328 |
| | | GB 2002-30086 | A | 20021224 |
| | | GB 2003-1916 | A | 20030128 |
| | | CN 2003-811739 | A3 | 20030326 |
| | | JP 2003-580299 | A3 | 20030326 |
| | | WO 2003-GB1306 | W | 20030326 |
| | | US 2004-508675 | A1 | 20040922 |

OTHER SOURCE(S): MARPAT 139:307787
 GI



AB The title compds. [I; G1, G2 = halo; X1 = a bond, O; R1 = H, alkyl, haloalkyl, etc.; X2 = a bond, $(CR_2R_3)_m$ ($m = 1-6$; R2, R3 = H, OH, alkyl, hydroxyalkyl); Q1 = (un)substituted cycloalkyl, heterocyclyl] and their pharmaceutically acceptable salts, useful as an antiproliferative agent in the prevention or treatment of tumors which are sensitive to inhibition of erbB receptor tyrosine kinases, were prepared and formulated. Thus, reacting 4-(3-chloro-2-fluoroanilino)-6-hydroxy-7-methoxyquinazoline (preparation given) with 1-methyl-3-pyrrolidinol in the presence of PPh₃ and di-tert-Bu azodicarboxylate in DCM afforded 16% I.HCl [G1 = F; G2 = Cl; X1 = O; R1 = Me; X2 = a bond; Q1 = 1-methylpyrrolidin-3-yl]. The compds. I showed IC₅₀ in the range of 0.001-10 μ M in EGFR tyrosine kinase phosphorylation assay.

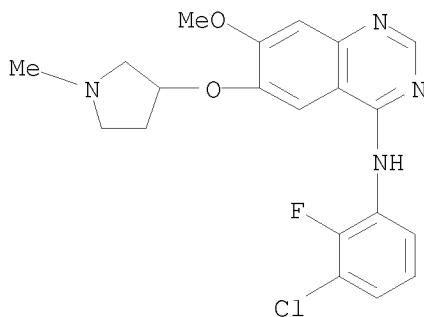
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612501-11-8P 612501-14-1P 612501-18-5P
612501-22-1P 612501-23-2P 612501-32-3P
612501-44-7P 612501-84-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 4-anilinoquinazolines as antiproliferative agents)

RN 612500-77-3 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(1-methyl-3-pyrrolidinyl)oxy]-, hydrochloride (1:1) (CA INDEX NAME)

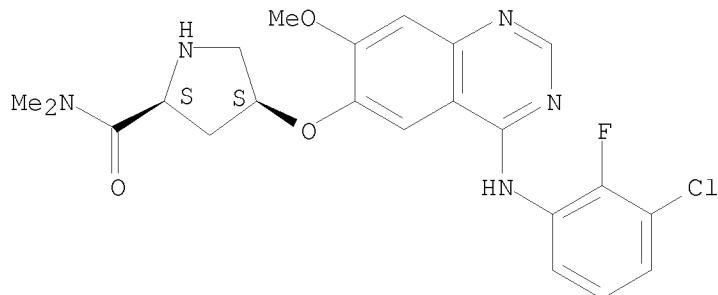


● HCl

RN 612501-00-5 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N-dimethyl-, (2S,4S)- (CA INDEX NAME)

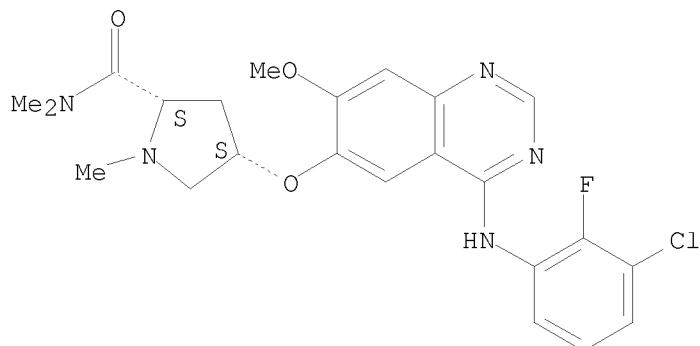
Absolute stereochemistry.



RN 612501-01-6 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quiazolinyl]oxy)-N,N,1-trimethyl-, (2S,4S)- (CA INDEX NAME)

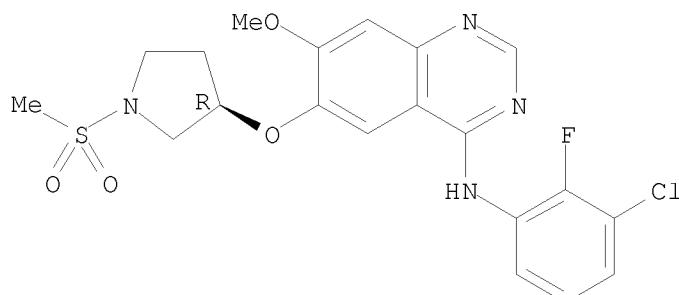
Absolute stereochemistry.



RN 612501-05-0 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3R)-1-(methylsulfonyl)-3-pyrrolidinyl]oxy- (CA INDEX NAME)

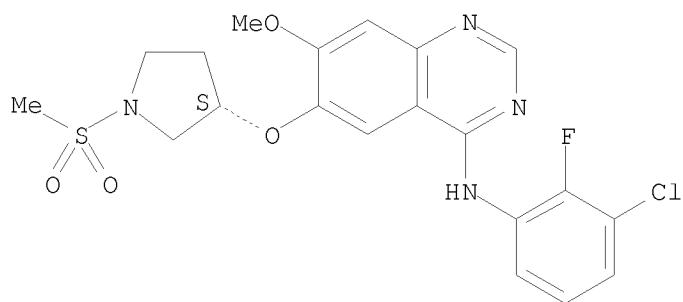
Absolute stereochemistry.



RN 612501-06-1 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3S)-1-(methylsulfonyl)-3-pyrrolidinyl]oxy- (CA INDEX NAME)

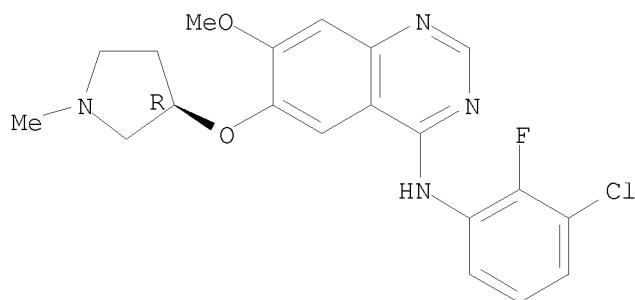
Absolute stereochemistry.



RN 612501-10-7 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3R)-1-methyl-3-pyrrolidinyl]oxy- (CA INDEX NAME)

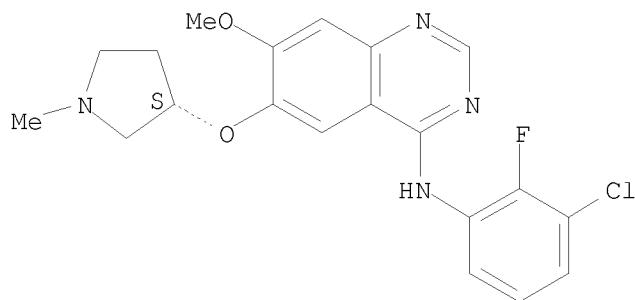
Absolute stereochemistry.



RN 612501-11-8 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3S)-1-methyl-3-pyrrolidinyl]oxy- (CA INDEX NAME)

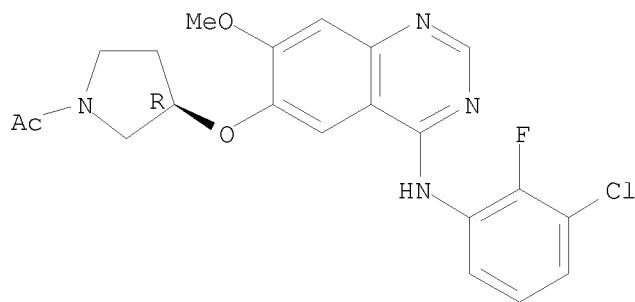
Absolute stereochemistry.



RN 612501-14-1 CAPLUS

CN Ethanone, 1-[(3R)-3-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-pyrrolidinyl]- (CA INDEX NAME)

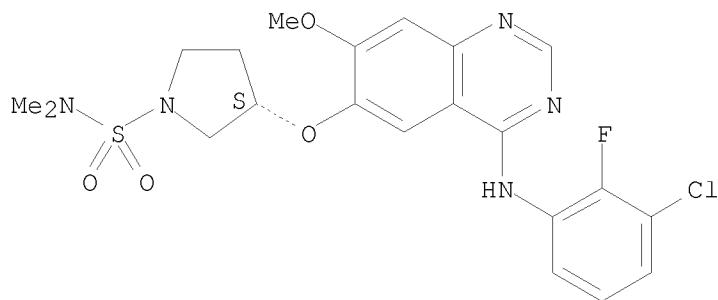
Absolute stereochemistry.



RN 612501-18-5 CAPLUS

CN 1-Pyrrolidinesulfonamide, 3-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy)-N,N-dimethyl-, (3S)- (CA INDEX NAME)

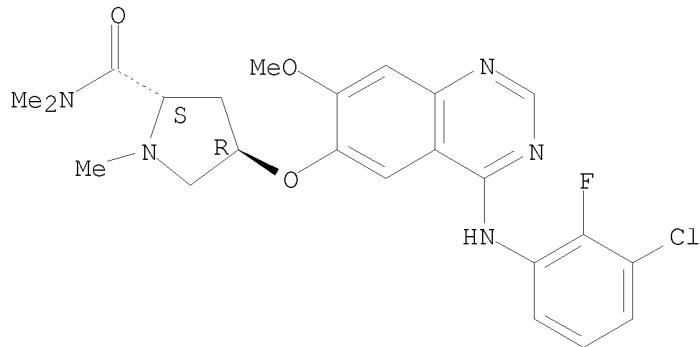
Absolute stereochemistry.



RN 612501-22-1 CAPLUS

CN 2-Pyrrolidinecarboxamide, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-N,N,1-trimethyl-, (2S,4R)- (CA INDEX NAME)

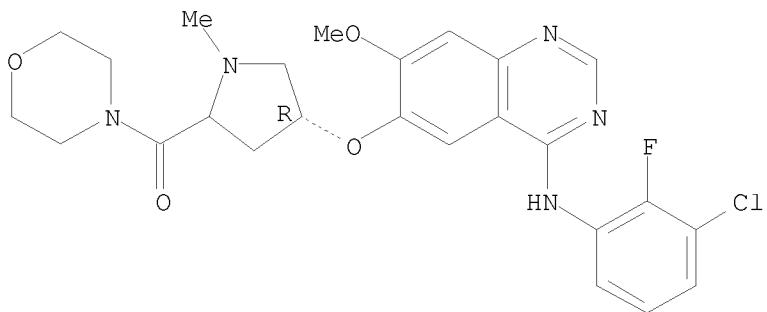
Absolute stereochemistry.



RN 612501-23-2 CAPLUS

CN Methanone, [(4R)-4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-2-pyrrolidinyl]-4-morpholinyl- (CA INDEX NAME)

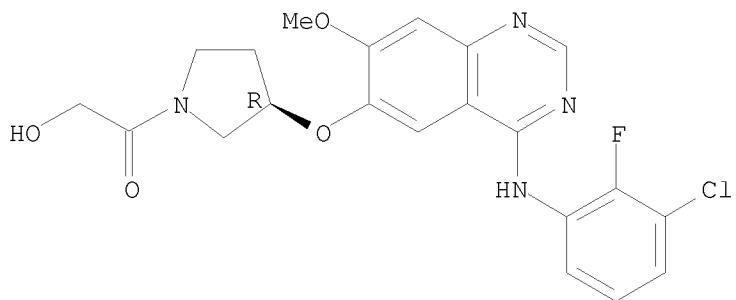
Absolute stereochemistry.



RN 612501-32-3 CAPLUS

CN Ethanone, 1-[(3R)-3-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-2-hydroxy- (CA INDEX NAME)

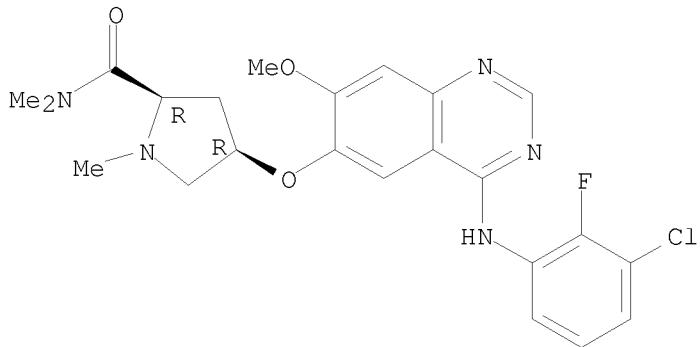
Absolute stereochemistry.



RN 612501-44-7 CAPLUS

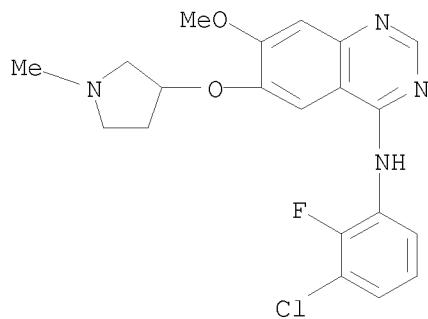
CN 2-Pyrrolidinecarboxamide, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-N,N,1-trimethyl-, (2R,4R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 612501-84-5 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(1-methyl-3-pyrrolidinyl)oxy]- (CA INDEX NAME)



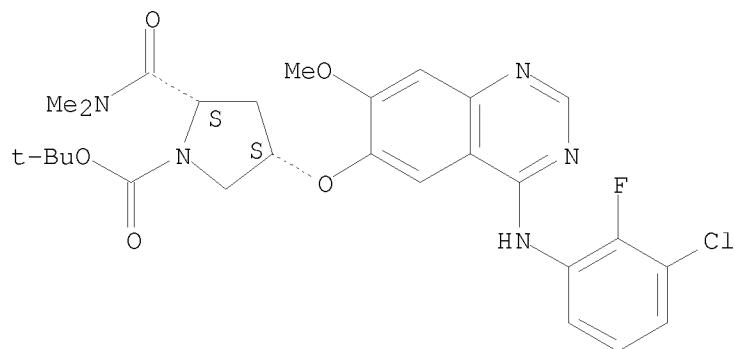
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 612501-72-1P 612501-73-2P 612501-74-3P
 612501-75-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 4-anilinoquinazolines as antiproliferative agents)

RN 612501-54-9 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-2-[(dimethylamino)carbonyl]-, 1,1-dimethylethyl ester, (2S,4S)- (CA INDEX NAME)

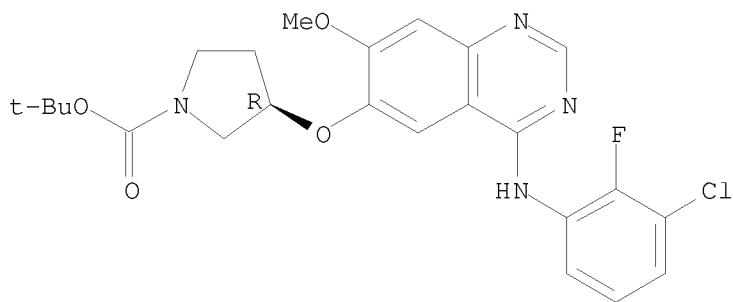
Absolute stereochemistry.



RN 612501-57-2 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1,1-dimethylethyl ester, (3R)- (CA INDEX NAME)

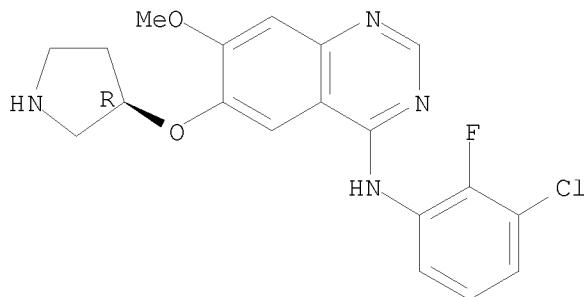
Absolute stereochemistry.



RN 612501-58-3 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3R)-3-pyrrolidinyl]oxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

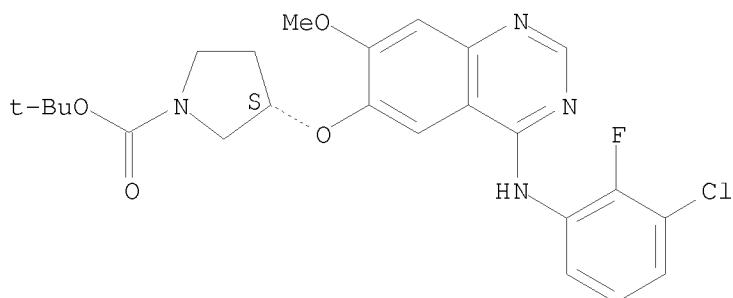


● HCl

RN 612501-60-7 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

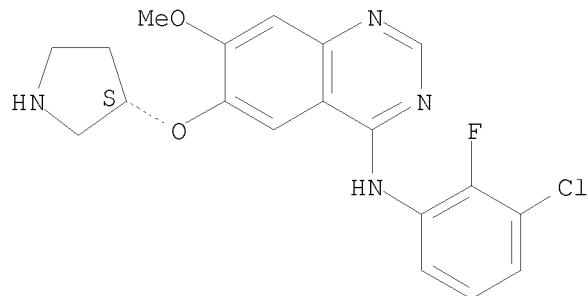
Absolute stereochemistry.



RN 612501-61-8 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-2-fluorophenyl)-7-methoxy-6-[(3S)-3-pyrrolidinyl]oxy-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

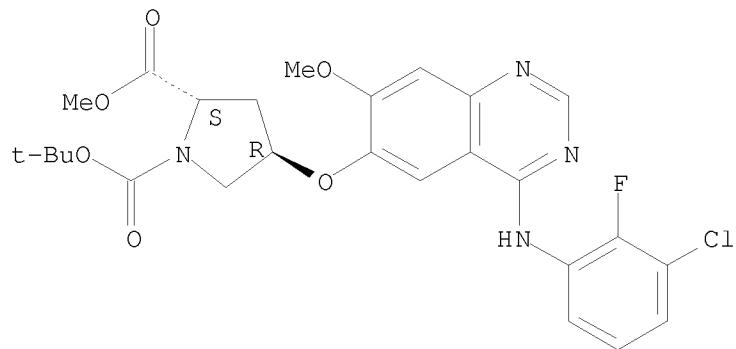


● HCl

RN 612501-71-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-, 1-(1,1-dimethylethyl) 2-methyl ester, (2S,4R)- (CA INDEX NAME)

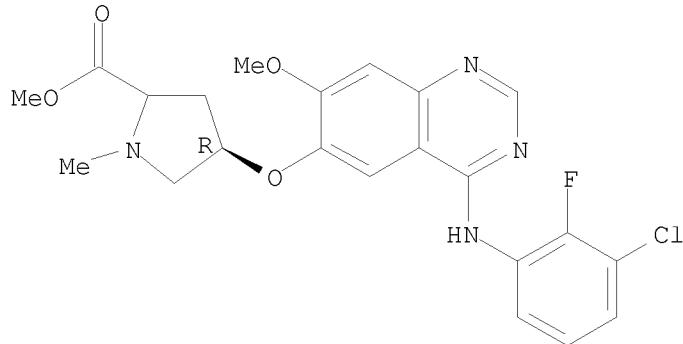
Absolute stereochemistry.



RN 612501-72-1 CAPLUS

CN Proline, 4-[(4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl)oxy]-1-methyl-, methyl ester, (4R)- (9CI) (CA INDEX NAME)

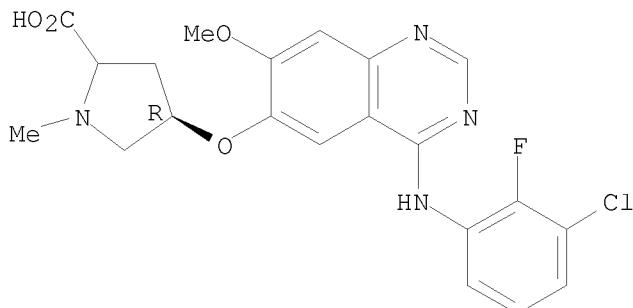
Absolute stereochemistry.



RN 612501-73-2 CAPLUS

CN Proline, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-, (4R)- (9CI) (CA INDEX NAME)

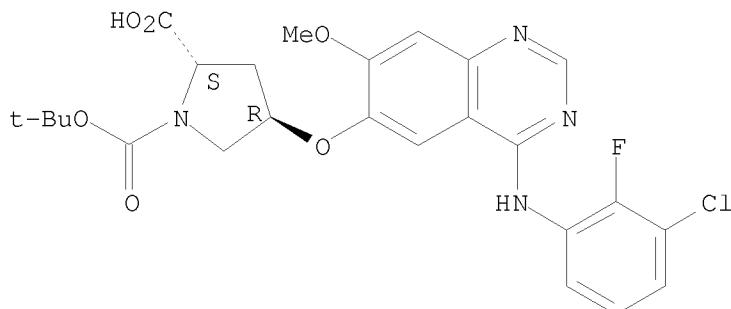
Absolute stereochemistry.



RN 612501-74-3 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1-(1,1-dimethylethyl) ester, (2S,4R)- (CA INDEX NAME)

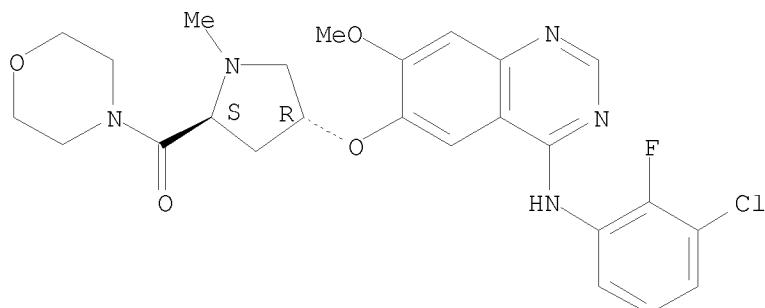
Absolute stereochemistry.



RN 612501-75-4 CAPLUS

CN Methanone, [(2S,4R)-4-[[4-[(3-chloro-2-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-methyl-2-pyrrolidinyl]-4-morpholinyl- (CA INDEX NAME)

Absolute stereochemistry.

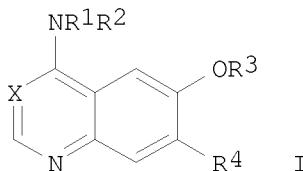


RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:796492 CAPLUS
 DOCUMENT NUMBER: 139:307786
 TITLE: Preparation of 4-(phenylamino)quinazolines as inhibitors of EGF-receptor kinase
 INVENTOR(S): Himmelsbach, Frank; Jung, Birgit; Solca, Flavio
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
 SOURCE: PCT Int. Appl., 148 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|-------------|
| WO 2003082290 | A1 | 20031009 | WO 2003-EP3062 | 20030325 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| DE 10214412 | A1 | 20031009 | DE 2002-10214412 | 20020330 |
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| JP 2005529090 | T | 20050929 | JP 2003-579827 | 20030325 |
| NZ 536114 | A | 20071130 | NZ 2003-536114 | 20030325 |
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| | | | WO 2003-EP3062 | W 20030325 |
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OTHER SOURCE(S): MARPAT 139:307786
 GI



AB Title compds. [I; R1 = H, C1-4 alkyl; R2 = (substituted) Ph, 1-phenylethyl; R3 = (amino-substituted) cyclobutyl, cyclopentyl, cyclohexyl; R4 = H, F, Cl, Br, alkoxy, (fluorinated) OMe, OCH₂CH₃, (substituted) alkyloxy, etc.; X = N, cyano-substituted CH], tautomers, stereoisomers, mixts., and salts thereof, especially the physiol. acceptable salts thereof with organic and inorg. acids, were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-hydroxy-7-methoxyquinazoline in MeCN was treated with (R)-3-hydroxytetrahydrofuran and Ph₃P followed by stirring with di-Et azodiformate over night at room temperature to give 15% 4-[(3-chloro-4-fluorophenyl)amino]-6-((S)-tetrahydrofuran-3-yloxy)-7-methoxyquinazoline. The latter inhibited EGF-receptor kinase with IC₅₀ = 0.13 nM.

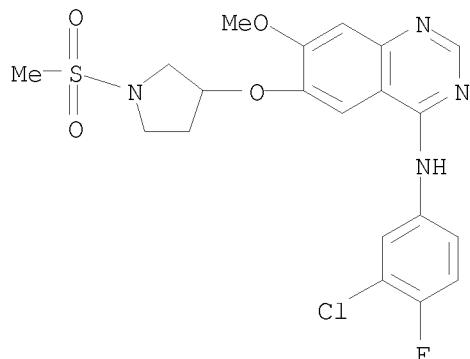
IT 1053774-97-2 1072544-68-3 1072544-69-4
1072544-70-7 1072544-71-8

RL: PRPH (Prophetic)

(Preparation of 4-(phenylamino)quinazolines as inhibitors of EGF-receptor kinase)

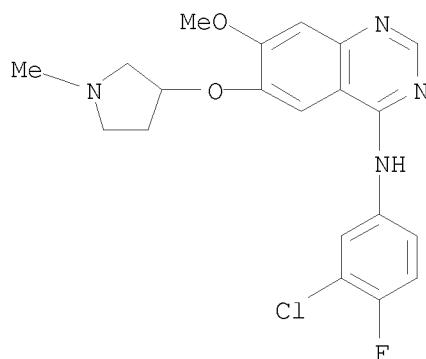
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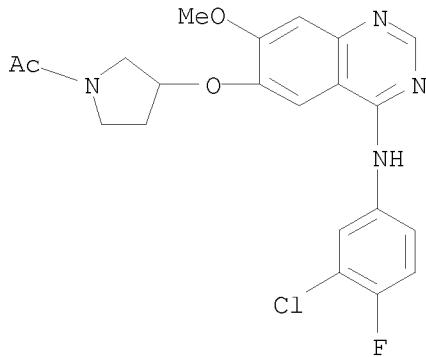
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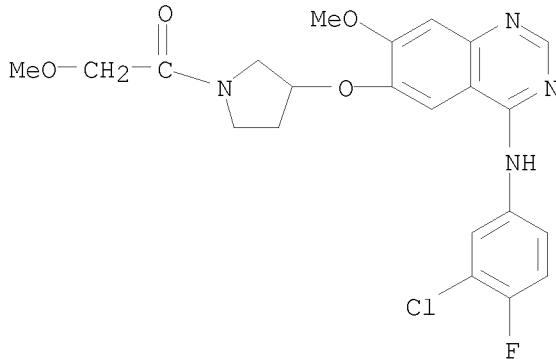
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CN Ethanone, 1-[3-[(4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]- (CA INDEX NAME)



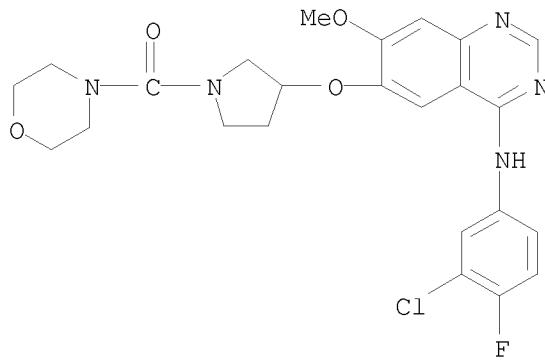
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CN Ethanone, 1-[3-[(4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-2-methoxy- (CA INDEX NAME)



RN 1072544-71-8 CAPLUS

CN Methanone, [3-[(4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-1-pyrrolidinyl]-4-morpholinyl- (CA INDEX NAME)



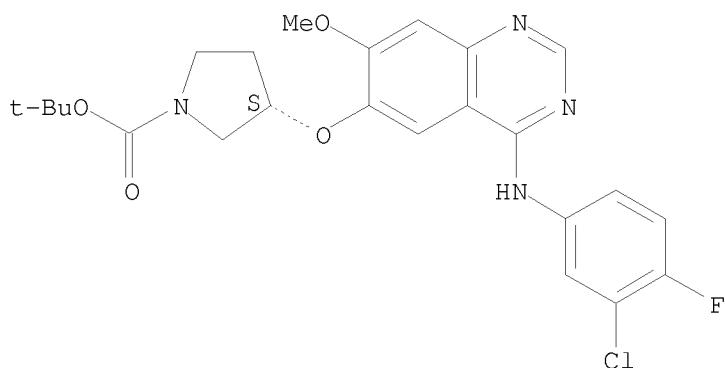
IT 610302-20-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of (phenylamino)quinazolines as inhibitors of EGF-receptor kinase)

RN 610302-20-0 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]oxy]-, 1,1-dimethylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



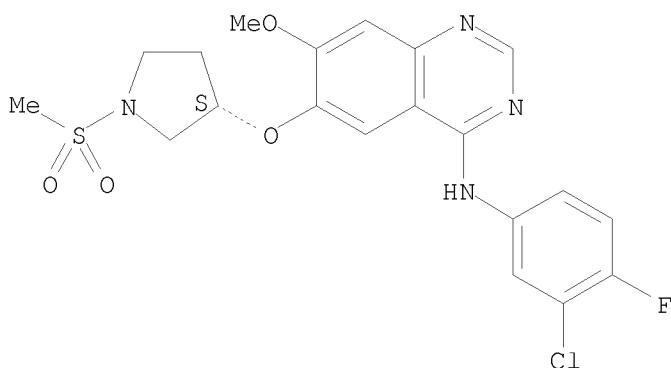
IT 610302-26-6P 610303-04-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of (phenylamino)quinazolines as inhibitors of EGF-receptor kinase)

RN 610302-26-6 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[(3S)-1-(methylsulfonyl)-3-pyrrolidinyl]oxy- (CA INDEX NAME)

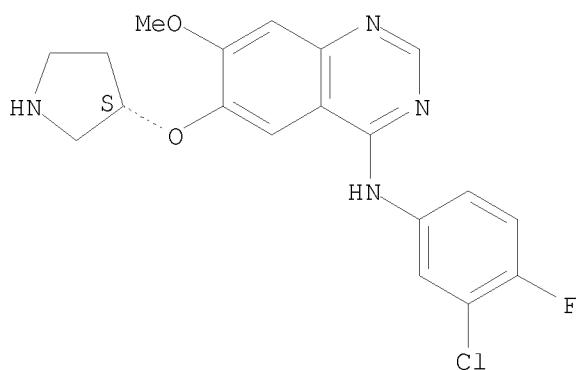
Absolute stereochemistry.



RN 610303-04-3 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[(3S)-3-pyrrolidinyl]oxy-, hydrochloride (1:2) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HC1

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

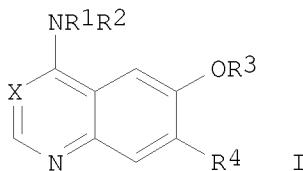
L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:793441 CAPLUS
DOCUMENT NUMBER: 139:292268
TITLE: Preparation of bicyclic heterocycles especially quinazolines as inhibitors of EGF-receptor kinase
INVENTOR(S): Himmelsbach, Frank; Jung, Birgit; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: Ger. Offen., 38 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------|
| DE 10214412 | A1 | 20031009 | DE 2002-10214412 | 20020330 |
| CA 2476008 | A1 | 20031009 | CA 2003-2476008 | 20030325 |
| WO 2003082290 | A1 | 20031009 | WO 2003-EP3062 | 20030325 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003226705 | A1 | 20031013 | AU 2003-226705 | 20030325 |
| AU 2003226705 | B2 | 20081106 | | |
| BR 2003008902 | A | 20050104 | BR 2003-8902 | 20030325 |
| EP 1492536 | A1 | 20050105 | EP 2003-745271 | 20030325 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1642552 | A | 20050720 | CN 2003-807242 | 20030325 |
| JP 2005529090 | T | 20050929 | JP 2003-579827 | 20030325 |
| NZ 536114 | A | 20071130 | NZ 2003-536114 | 20030325 |

| | | | | |
|------------------------|----|----------|------------------|-------------|
| US 20040048880 | A1 | 20040311 | US 2003-400370 | 20030327 |
| US 6924285 | B2 | 20050802 | | |
| IN 2004DN02255 | A | 20070112 | IN 2004-DN2255 | 20040802 |
| NO 2004003997 | A | 20041027 | NO 2004-3997 | 20040923 |
| MX 2004009536 | A | 20050125 | MX 2004-9536 | 20040930 |
| US 20050182043 | A1 | 20050818 | US 2005-83247 | 20050317 |
| US 7119084 | B2 | 20061010 | | |
| US 20060270672 | A1 | 20061130 | US 2006-497727 | 20060802 |
| US 20090036676 | A1 | 20090205 | US 2008-72510 | 20080226 |
| IN 2008DN07026 | A | 20080912 | IN 2008-DN7026 | 20080818 |
| PRIORITY APPLN. INFO.: | | | DE 2002-10214412 | A 20020330 |
| | | | US 2002-381176P | P 20020516 |
| | | | DE 2002-10231711 | A 20020713 |
| | | | WO 2003-EP3062 | W 20030325 |
| | | | US 2003-400370 | A3 20030327 |
| | | | IN 2004-DN2255 | A3 20040802 |
| | | | US 2005-83247 | A1 20050317 |
| | | | US 2006-497727 | B1 20060802 |

OTHER SOURCE(S): MARPAT 139:292268

GI



AB Title compds. [I; R1 = H, C1-4 alkyl; R2 = (substituted) Ph, 1-phenylethyl; R3 = (amino-substituted) cyclobutyl, cyclopentyl, cyclohexyl; R4 = H, F, Cl, Br, alkoxy, (fluorinated) OMe, OCH2CH3, (substituted) alkyloxy, etc.; X = N, cyano-substituted CH], tautomers, stereoisomers, and salts thereof, especially the physiol. acceptable salts thereof with inorg. or organic acids, were prepared. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-hydroxy-7-methoxyquinazoline in MeCN was treated with (R)-3-hydroxytetrahydrofuran and Ph3P followed by stirring with di-Et azodiformate over night at room temperature to give 15% 4-[(3-chloro-4-fluorophenyl)amino]-6-((S)-tetrahydrofuran-3-yloxy)-7-methoxyquinazoline. The latter inhibited EGF-receptor kinase with IC50 = 0.13 nM.

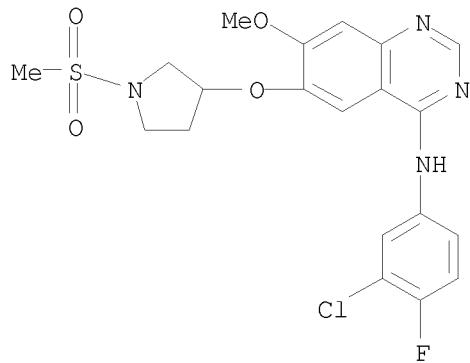
IT 1053774-97-2

RL: PRPH (Prophetic)

(Preparation of bicyclic heterocycles especially quinazolines as inhibitors of EGF-receptor kinase)

RN 1053774-97-2 CAPLUS

CN 4-Quinazolinamine, N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[(1-methylsulfonyl)-3-pyrrolidinyl]oxy]- (CA INDEX NAME)



L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:434373 CAPLUS

DOCUMENT NUMBER: 139:6886

TITLE: Preparation of quinazoline derivatives for the treatment of T cell mediated diseases

INVENTOR(S): Moore, Nelly Corine; Oldham, Keith

PATENT ASSIGNEE(S): Astrazeneca A.B., Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 217 pp.

CODEN: PIXXD2

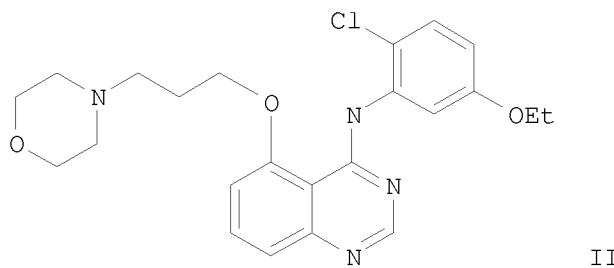
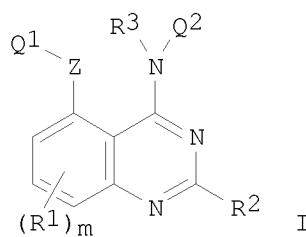
DOCUMENT TYPE: Patent

LANGUAGE: English

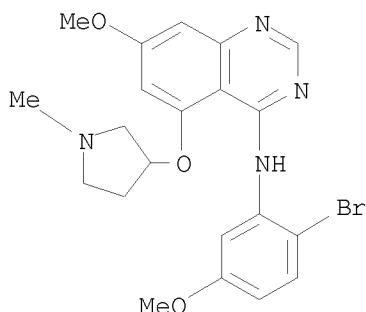
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|----------|-----------------|------------|
| WO 2003045395 | A1 | 20030605 | WO 2002-GB5222 | 20021120 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002343047 | A1 | 20030610 | AU 2002-343047 | 20021120 |
| EP 1450808 | A1 | 20040901 | EP 2002-779708 | 20021120 |
| EP 1450808 | B1 | 20050615 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| AT 297733 | T | 20050715 | AT 2002-779708 | 20021120 |
| US 20050038050 | A1 | 20050217 | US 2004-496587 | 20040524 |
| US 7160891 | B2 | 20070109 | | |
| PRIORITY APPLN. INFO.: | | | GB 2001-28108 | A 20011123 |
| | | | WO 2002-GB5222 | W 20021120 |
| OTHER SOURCE(S): | MARPAT | 139:6886 | | |
| GI | | | | |



- AB Title compds. I [$m = 0-3$; $R1 = \text{halo, CF}_3, \text{CN, NO}_2, \text{etc.}; R2 = \text{H, alkyl; R3} = \text{H, alkyl; Z} = \text{bond, O, SOO-2, amino, etc.; Q1} = \text{aryl(alkyl), cycloalkyl, cycloalkenyl, heteroaryl, etc.; Q2} = \text{phenyl}] \text{ are prepared. For instance, 4-[2-chloro-5-ethoxyphenyl]amino]-5-hydroxy-7-methoxyquinazoline (preparation given) was coupled to 4-(3-hydroxypropyl)morpholine (CH}_2\text{Cl}_2, \text{Ph}_3\text{P, t-BuO}_2\text{C-N=N-CO}_2\text{Bu-t}) \text{ to give II. I are useful for the prevention or treatment of T cell mediated diseases.}$
- IT 379231-23-9P, 7-Methoxy-5-[[N-methylpyrrolidin-3-yl]oxy]-4-[[2-bromo-5-methoxyphenyl]amino]quinazoline dihydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quinazoline derivs. for treatment of T cell mediated diseases)
- RN 379231-23-9 CAPLUS
- CN 4-Quinazolinamine, N-(2-bromo-5-methoxyphenyl)-7-methoxy-5-[(1-methyl-3-pyrrolidinyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



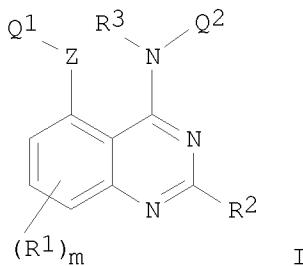
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2001:904160 CAPLUS
 DOCUMENT NUMBER: 136:20087
 TITLE: Preparation of 4-anilinoquinazoline derivatives for the treatment of tumors
 INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick
 PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
 SOURCE: PCT Int. Appl., 234 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2001094341 | A1 | 20011213 | WO 2001-GB2424 | 20010601 |
| WO 2001094341 | A9 | 20030417 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2407371 | A1 | 20011213 | CA 2001-2407371 | 20010601 |
| EP 1292594 | A1 | 20030319 | EP 2001-934176 | 20010601 |
| EP 1292594 | B1 | 20040901 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001011335 | A | 20030610 | BR 2001-11335 | 20010601 |
| HU 2003001046 | A2 | 20030828 | HU 2003-1046 | 20010601 |
| HU 2003001046 | A3 | 20081229 | | |
| JP 2003535859 | T | 20031202 | JP 2002-501890 | 20010601 |
| JP 3774438 | B2 | 20060517 | | |
| EE 200200673 | A | 20040615 | EE 2002-673 | 20010601 |
| NZ 522204 | A | 20040730 | NZ 2001-522204 | 20010601 |
| AT 275145 | T | 20040915 | AT 2001-934176 | 20010601 |
| PT 1292594 | T | 20041231 | PT 2001-934176 | 20010601 |
| ES 2225545 | T3 | 20050316 | ES 2001-934176 | 20010601 |
| AU 2001260482 | B2 | 20050609 | AU 2001-260482 | 20010601 |
| RU 2276151 | C2 | 20060510 | RU 2002-135617 | 20010601 |
| CN 100345844 | C | 20071031 | CN 2001-810830 | 20010601 |
| TW 288748 | B | 20071021 | TW 2001-90113714 | 20010606 |
| IN 2002MN01457 | A | 20050304 | IN 2002-MN1457 | 20021021 |
| US 20040214841 | A1 | 20041028 | US 2002-275382 | 20021105 |
| US 7049438 | B2 | 20060523 | | |
| ZA 2002009122 | A | 20040209 | ZA 2002-9122 | 20021108 |
| MX 2002011765 | A | 20030410 | MX 2002-11765 | 20021128 |
| BG 107332 | A | 20030731 | BG 2002-107332 | 20021128 |
| NO 2002005792 | A | 20021202 | NO 2002-5792 | 20021202 |
| NO 324838 | B1 | 20071217 | | |
| KR 807162 | B1 | 20080227 | KR 2002-716508 | 20021204 |

| | | | | |
|------------------------|----|----------|----------------|-------------|
| HK 1053115 | A1 | 20050408 | HK 2003-105395 | 20030725 |
| KR 2008015055 | A | 20080215 | KR 2008-702129 | 20080125 |
| PRIORITY APPLN. INFO.: | | | EP 2000-401581 | A 20000606 |
| | | | EP 2001-400297 | A 20010207 |
| | | | EP 2001-400565 | A 20010305 |
| | | | WO 2001-GB2424 | W 20010601 |
| | | | KR 2002-716508 | A3 20021204 |

OTHER SOURCE(S): MARPAT 136:20087
GI



AB The invention concerns quinazoline derivs. (I; e.g. 4-(2-chloro-5-methoxyanilino)-7-methoxy-5-(3-morpholinopropoxy)quinazoline (1)), processes for their preparation, pharmaceutical compns. containing them and

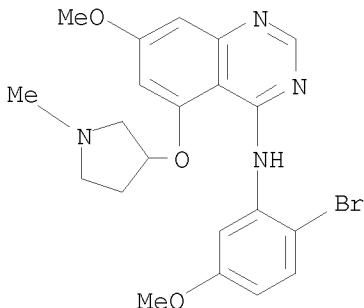
their use in the manufacture of a medicament for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease. Although biol. assay methods are described, no test results are reported. It is believed that the antitumor activity is due to inhibition of one or more of the non-receptor tyrosine-specific protein kinases of the Src family that are involved in the signal transduction steps that lead to the invasiveness and migratory ability of metastasizing tumor cells. In I, according to the 1st claim, m = 0-3; each R1 = halo, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or Q3-X1- (X1 = direct bond, O, S, SO, SO₂, N(R4), CO, CH(OR4), CON(R4), N(R4)CO, SO₂N(R4), N(R4)SO₂, OC(R4)₂, SC(R4)₂ and N(R4)C(R4)₂ (R4 = H or (1-6C)alkyl) and Q3 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-, (1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl), or (R1)_m is (1-3C)alkylenedioxy, with addnl. optional substitution and/or insertion possible. R2 = H or (1-6C)alkyl; R3 = H or (1-6C)alkyl; Z = direct bond, O, S, SO, SO₂, N(R11), CO, CH(OR11), CON(R11), N(R11)CO, SO₂N(R11), N(R11)SO₂, OC(R11)₂, SC(R11)₂ and N(R11)C(R11)₂ (R11 = H, or (1-6C)alkyl). Q1 = aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl,

(3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or, when Z is a direct bond or O, Q1 may be (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, halo-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di[(1-6C)alkyl]amino-(1-6C)alkyl, (1-6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl or (1-6C)alkylsulfonyl-(1-6C)alkyl, with addnl. optional substitution and/or insertion possible. Q2 = substituted Ph. More than 50 example preps. are included. For example, 1 was obtained by adding di-tert-Bu azodicarboxylate (0.208 g) dropwise to a stirred mixture of 4-(2-chloro-5-methoxyanilino)-5-hydroxy-7-methoxyquinazoline (0.2 g), 4-(3-hydroxypropyl)morpholine, PPh₃ (0.237 g) and CH₂Cl₂ (3 mL). The reaction mixture was stirred at ambient temperature for 1 h.

IT 379231-23-9P, 4-(2-Bromo-5-methoxyanilino)-7-methoxy-5-[(N-methylpyrrolidin-3-yl)oxy]quinazoline dihydrochloride
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of anilinoquinazoline derivs. for treatment of tumors)

RN 379231-23-9 CAPLUS

CN 4-Quinazolinamine, N-(2-bromo-5-methoxyphenyl)-7-methoxy-5-[(1-methyl-3-pyrrolidinyl)oxy]-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 13:25:53 ON 23 FEB 2009)

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 L1 STRUCTURE uploaded
 L2 177 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:26:49 ON 23 FEB 2009

FILE 'REGISTRY' ENTERED AT 13:26:55 ON 23 FEB 2009

FILE 'CAPLUS' ENTERED AT 13:26:56 ON 23 FEB 2009

10/ 573,352

L3 8 S L2

=> log y
COST IN U.S. DOLLARS

FULL ESTIMATED COST

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ENTRY | TOTAL
SESSION |
|----------------------|------------------|
| XXXXXXXXXXXXXXXXXXXX | |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

| SINCE FILE
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SESSION |
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STN INTERNATIONAL LOGOFF AT 13:28:33 ON 23 FEB 2009